```
=> fil capl; d que l6; d que l10; s l6 or l10
FILE 'CAPLUS' ENTERED AT 15:17:06 ON 13 FEB 2003
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inventors

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FILE COVERS 1907 - 13 Feb 2003  VOL 138 ISS 7
FILE LAST UPDATED: 12 Feb 2003  (20030212/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L1          485 SEA FILE=CAPLUS ABB=ON  MYERS T?/AU
L2           91 SEA FILE=CAPLUS ABB=ON  PIEPER R?/AU
L3         5673 SEA FILE=CAPLUS ABB=ON  TAYLOR J?/AU
L4          184 SEA FILE=CAPLUS ABB=ON  STEINER S?/AU
L5          908 SEA FILE=CAPLUS ABB=ON  ANDERSON N?/AU
L6            1 SEA FILE=CAPLUS ABB=ON  L1 AND L2 AND L3 AND L4 AND L5


L1          485 SEA FILE=CAPLUS ABB=ON  MYERS T?/AU
L2           91 SEA FILE=CAPLUS ABB=ON  PIEPER R?/AU
L3         5673 SEA FILE=CAPLUS ABB=ON  TAYLOR J?/AU
L4          184 SEA FILE=CAPLUS ABB=ON  STEINER S?/AU
L5          908 SEA FILE=CAPLUS ABB=ON  ANDERSON N?/AU
L7         4153 SEA FILE=CAPLUS ABB=ON  PROTEOM?
L9           29 SEA FILE=CAPLUS ABB=ON  ((L1 AND (L2 OR L3 OR L4 OR L5)) OR
                (L2 AND (L3 OR L4 OR L5)) OR (L3 AND (L4 OR L5)) OR (L4 AND
                L5))
L10           8 SEA FILE=CAPLUS ABB=ON  L9 AND L7


L149          8 L6 OR L10

=> fil medl; d que l53

FILE 'MEDLINE' ENTERED AT 15:17:07 ON 13 FEB 2003

 FILE LAST UPDATED: 12 FEB 2003 (20030212/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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L45          384 SEA FILE=MEDLINE ABB=ON  MYERS T?/AU
L46           85 SEA FILE=MEDLINE ABB=ON  PIEPER R?/AU
L47         4166 SEA FILE=MEDLINE ABB=ON  TAYLOR J?/AU
L48          205 SEA FILE=MEDLINE ABB=ON  STEINER S?/AU
L49          963 SEA FILE=MEDLINE ABB=ON  ANDERSON N?/AU
L50         3026 SEA FILE=MEDLINE ABB=ON  PROTEOM?
L51        71919 SEA FILE=MEDLINE ABB=ON  DRUG EVALUATION, PRECLINICAL+NT/CT
L52         8646 SEA FILE=MEDLINE ABB=ON  DRUG DESIGN/CT
L53            2 SEA FILE=MEDLINE ABB=ON  (L45 OR L46 OR L47 OR L48 OR L49) AND
                  L50 AND (L51 OR L52)


=> fil embase; d que l100

FILE 'EMBASE' ENTERED AT 15:17:08 ON 13 FEB 2003
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 FILE COVERS 1974 TO 7 Feb 2003 (20030207/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L80          325 SEA FILE=EMBASE ABB=ON  MYERS T?/AU
L81           81 SEA FILE=EMBASE ABB=ON  PIEPER R?/AU
L82         3482 SEA FILE=EMBASE ABB=ON  TAYLOR J?/AU
L83          163 SEA FILE=EMBASE ABB=ON  STEINER S?/AU
L84          616 SEA FILE=EMBASE ABB=ON  ANDERSON N?/AU
L85         2659 SEA FILE=EMBASE ABB=ON  PROTEOM?
L86           16 SEA FILE=EMBASE ABB=ON  (L80 OR L81 OR L82 OR L83 OR L84) AND
                  L85
L87        61966 SEA FILE=EMBASE ABB=ON  DRUG SCREENING/CT
L88         8099 SEA FILE=EMBASE ABB=ON  DRUG DESIGN/CT
L89         7161 SEA FILE=EMBASE ABB=ON  DISEASE MARKER/CT
L90        18616 SEA FILE=EMBASE ABB=ON  DRUG TARGETING+NT/CT
L91        45089 SEA FILE=EMBASE ABB=ON  OBESITY+NT/CT
L92        24687 SEA FILE=EMBASE ABB=ON  OSTEOPOROSIS+NT/CT
L93       142687 SEA FILE=EMBASE ABB=ON  DIABETES MELLITUS+NT/CT
L94        13320 SEA FILE=EMBASE ABB=ON  OSTEOARTHRITIS+NT/CT
L95       164369 SEA FILE=EMBASE ABB=ON  HYPERTENSION+NT/CT
L96        18623 SEA FILE=EMBASE ABB=ON  ANTIHYPERTENSIVE AGENT/CT
L97          347 SEA FILE=EMBASE ABB=ON  ANTIOBESITY AGENT/CT
L98         4867 SEA FILE=EMBASE ABB=ON  ANTIDIABETIC AGENT/CT
L99            1 SEA FILE=EMBASE ABB=ON  ANTIOSTEOPOROTIC AGENT/CT
L100           3 SEA FILE=EMBASE ABB=ON  L86 AND (L87 OR L88 OR L89 OR L90 OR
                  L91 OR L92 OR L93 OR L94 OR L95 OR L96 OR L97 OR L98 OR L99)


=> fil wpids; d que l126

FILE 'WPIDS' ENTERED AT 15:17:08 ON 13 FEB 2003
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FILE LAST UPDATED:          11 FEB 2003      <20030211/UP>
MOST RECENT DERWENT UPDATE:     200310        <200310/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

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L119         127 SEA FILE=WPIDS ABB=ON  MYERS T?/AU
L120          35 SEA FILE=WPIDS ABB=ON  PIEPER R?/AU
L121        1203 SEA FILE=WPIDS ABB=ON  TAYLOR J?/AU
L122          37 SEA FILE=WPIDS ABB=ON  STEINER S?/AU
L123         218 SEA FILE=WPIDS ABB=ON  ANDERSON N?/AU
L124         276 SEA FILE=WPIDS ABB=ON  PROTEOM?
L126           4 SEA FILE=WPIDS ABB=ON  (L119 OR L120 OR L121 OR L122 OR L123)
                 AND L124
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=> dup rem l53,l149,l100,l126 ;
FILE 'MEDLINE' ENTERED AT 15:17:33 ON 13 FEB 2003

FILE 'CAPLUS' ENTERED AT 15:17:33 ON 13 FEB 2003
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FILE 'WPIDS' ENTERED AT 15:17:33 ON 13 FEB 2003
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PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L149
PROCESSING COMPLETED FOR L100
PROCESSING COMPLETED FOR L126
L150          12 DUP REM L53 L149 L100 L126 (5 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE MEDLINE
                 ANSWERS '3-9' FROM FILE CAPLUS
                 ANSWER '10' FROM FILE EMBASE
                 ANSWERS '11-12' FROM FILE WPIDS
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=> d ibib ab 1-12

L150 ANSWER 1 OF 12     MEDLINE                          DUPLICATE 4
ACCESSION NUMBER:    2001047596     MEDLINE
DOCUMENT NUMBER:     20534067   PubMed ID: 11083096
TITLE:               Pharmaceutical proteomics.
AUTHOR:              Steiner S; Anderson N L
CORPORATE SOURCE:    Large Scale Proteomics Corporation, Rockville, Maryland
                     20850-3338, USA.. sandra.steiner@lsbc.com
SOURCE:              ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2000) 919
```

48-51.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001206

AB Genomics and **proteomics** are today well established in drug discovery and, in combination with combinatorial chemistry and high-throughput screening, are helping to bring forward an unprecedented number of potential lead compounds. To avoid the generation of bottlenecks downstream in drug development, increasing pressure is arising to integrate these technologies into the development environment. **Proteomics** has demonstrated proof-of-concept in toxicology as shown by a number of successful applications in mechanistic toxicology and lead selection. The "technology wave" is now starting to impact the clinical phase of drug development. Expected benefits are optimized clinical trials based on the availability of biologically relevant markers of drug efficacy and safety.

L150 ANSWER 2 OF 12 MEDLINE
ACCESSION NUMBER: 2001010710 MEDLINE
DOCUMENT NUMBER: 20348809 PubMed ID: 10892720
TITLE: **Proteomics**: applications and opportunities in preclinical drug development.
AUTHOR: **Steiner S**; Witzmann F A
CORPORATE SOURCE: Large Scale Proteomics Corporation, Rockville, MD 20850, USA.. sandra.steiner@lsbc.com
SOURCE: ELECTROPHORESIS, (2000 Jun) 21 (11) 2099-104. Ref: 66
Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001026

AB Advances in DNA sequencing and the near-term availability of whole genome sequences for several pharmaceutically relevant organisms promise to dramatically alter the breadth and scale of high-throughput **proteomic** studies. The substantial amount of literature is available in the public domain, demonstrate the potential of **proteomics** in the preclinical phases of pharmaceutical development. Over the next few years, it is anticipated that functional genomics and **proteomics** will have major impacts on the clinical phases of drug development. Expected benefits are earlier proof-of-concept studies in man and increased efficiency of clinical trials through the availability of biologically relevant markers for drug efficacy and safety.

L150 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:220406 CAPLUS
DOCUMENT NUMBER: 136:244020
TITLE: Non-genetic based protein disease markers
INVENTOR(S): Rembert, Pieper; **Taylor, John, Jr.**; **Steiner, Sandra**; **Anderson, N. Leigh**; **Myers, Timothy**

Searched by Barb O'Bryen, STIC 308-4291

PATENT ASSIGNEE(S): Large Scale Proteomics Corporation, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022165	A1	20020321	WO 2001-US28268	20010912
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002072492	A1	20020613	US 2001-886271	20010622
AU 2001088973	A5	20020326	AU 2001-88973	20010912

PRIORITY APPLN. INFO.: US 2000-660242 A 20000912
US 2001-886271 A 20010622
WO 2001-US28268 W 20010912

AB The invention concerns protein disease markers for obesity, osteoporosis, diabetes, osteoarthritis and hypertension are disclosed. These markers are not inherited or of genetic origin as they were not found in identical twins of the affected individual. Methods and uses for diagnostic, therapeutic and drug discovery are disclosed.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2001:904571 CAPLUS
DOCUMENT NUMBER: 136:15220
TITLE: Using **proteomics** to identify protein markers of drug toxicity and efficacy in a patient and determining drug susceptibility prior to treatment
INVENTOR(S): **Anderson, N. Leigh; Steiner, Sandra**
PATENT ASSIGNEE(S): Large Scale Proteomics Corp., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094616	A1	20011213	WO 2001-US17751	20010601
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-585475 A2 20000602

AB Protein markers of toxicity and efficacy for drugs are detd. For example, methods and reagents are disclosed for detg. whether a patient receiving an antilipemic drug, esp. a statin or HMG-CoA reductase inhibiting drug, is experiencing drug efficacy and/or toxicity. Individual susceptibility is also detd. prior to treatment. Also, drug discovery of similar acting candidates and their likelihood of being toxic or effective is detd. by anal. of all proteins in a sample simultaneously by 2-dimensional gel electrophoresis. Another embodiment of the present invention is a database comprising a plurality of protein markers that differ by mol. wt., isoelec. point or correlation with a neg. or pos. phenotype before and after exposure to the drug.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:173674 CAPLUS
DOCUMENT NUMBER: 133:75
TITLE: Expression profiling in toxicology - potentials and limitations
AUTHOR(S): **Steiner, S.; Anderson, N. L.**
CORPORATE SOURCE: Large Scale Biology Corporation, Rockville, MD, USA
SOURCE: Toxicology Letters (2000), 112-113, 467-471
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with 16 refs. Recent progress in genomics and **proteomics** technologies has created a unique opportunity to significantly impact the pharmaceutical drug development processes. The perception that cells and whole organisms express specific inducible responses to stimuli such as drug treatment implies that unique expression patterns, mol. fingerprints, indicative of a drug's efficacy and potential toxicity are accessible. The integration into state-of-the-art toxicol. of assays allowing one to profile treatment-related changes in gene expression patterns promises new insights into mechanisms of drug action and toxicity. The benefits will be improved lead selection, and optimized monitoring of drug efficacy and safety in pre-clin. and clin. studies based on biol. relevant tissue and surrogate markers.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:450337 CAPLUS
DOCUMENT NUMBER: 137:2745
TITLE: Non-genetic based protein disease markers
INVENTOR(S): **Myers, Timothy G.; Pieper, Rembert ; Taylor, John; Steiner, Sandra; Anderson, N. Leigh**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U. S. Ser. No. 660,242.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002072492	A1	20020613	US 2001-886271	20010622
WO 2002022165	A1	20020321	WO 2001-US28268	20010912

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,

FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL,
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001088973 A5 20020326 AU 2001-88973 20010912
PRIORITY APPLN. INFO.: US 2000-660242 A2 20000912
US 2001-886271 A 20010622
WO 2001-US28268 W 20010912

AB The invention concerns protein disease markers for obesity, osteoporosis, diabetes, osteoarthritis and hypertension. These markers are not inherited or of genetic origin as they were not found in identical twins of the affected individual. Methods and uses for diagnostic, therapeutic and drug discovery are disclosed.

L150 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:468893 CAPLUS
DOCUMENT NUMBER: 133:159806
TITLE: **Proteomics** to display lovastatin-induced protein and pathway regulation in rat liver
AUTHOR(S): **Steiner, Sandra**; Gatlin, Christine L.; Lennon, John J.; McGrath, Andrew M.; Aponte, Angel M.; Makusky, Anthony J.; Rohrs, Maria C.; **Anderson, N. Leigh**
CORPORATE SOURCE: Large Scale Proteomics Corporation, Rockville, MD, 20850, USA
SOURCE: Electrophoresis (2000), 21(11), 2129-2137
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lovastatin is a lipid lowering agent that acts by inhibiting 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, a key regulatory enzyme in cholesterol biosynthesis. In this study the pattern of gene network regulation induced in hepatic proteins as a response to lovastatin treatment was analyzed by **proteomics**. In livers of male F344 rats treated with 1.6 mg/kg/day lovastatin or 150 mg/kg/day lovastatin for seven days, 36 proteins were found to be significantly altered ($p<0.001$) in relation to treatment. The changed proteins were classified according to their cellular function and participation in biochem. pathways. The following observations were made: (i) inhibition of HMG-CoA reductase provoked a regulatory response in the cholesterol synthesis pathway including the induction of cytosolic HMG-CoA synthase and of isopentenyl-diphosphate delta-isomerase, (ii) manipulation of the lipid metab. triggered alterations in key enzymes of the carbohydrate metab., and (iii) lovastatin treatment was assocd. with signs of toxicity as reflected by changes in a heterogeneous set of cellular stress proteins involved in functions such as cytoskeletal structure, calcium homeostasis, protease inhibition, cell signaling or apoptosis. These results present new insights into liver gene network regulations induced by lovastatin and illustrate a yet unexplored application of **proteomics** to discover new targets by anal. of existing drugs and the pathways that they regulate.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:468892 CAPLUS
DOCUMENT NUMBER: 133:187911
TITLE: Two-dimensional electrophoresis of liver proteins:

characterization of a drug-induced hepatomegaly in rats
AUTHOR(S): Newsholme, Stephen J.; Maleeff, Beverly F.; **Steiner, Sandra; Anderson, N. Leigh;** Schwartz, Lester W.
CORPORATE SOURCE: Safety Assessment, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Electrophoresis (2000), 21(11), 2122-2128
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two-dimensional electrophoresis (2-DE) of liver proteins was applied to further characterize an unusual drug-induced increase in hepatocellular rough endoplasmic reticulum (RER) in Sprague-Dawley rats given a substituted pyrimidine deriv. Abs. liver wts. of drug-treated rats (9.9 .+-. 0.4 g) increased above vehicle-treated controls (7.2 .+-. 0.2 g) by 37%. Light microscopy revealed diffuse granular basophilia of the hepatocellular cytoplasm, uncharacteristic of hepatocytes and suggested cells rich in ribosomes, which was confirmed by electron microscopy. Immunostaining for cell proliferation, viz., 5-bromo-2'-deoxyuridine (BrdU) and proliferating cell nuclear antigen (PCNA), indicated marked hepatocellular proliferative activity. 2-DE of solubilized liver using an ISO-DALT gel system indicated significant ($p<0.001$) quant. changes in at least 17 liver proteins (12 increased, 5 decreased) compared to controls. The protein with the largest increase was homologous to acute-phase reactant, contrapsin-like protein inhibitor-6. Other markedly upregulated proteins were methionine adenosyltransferase, a catalyst in methionine/ATP metab. and mitochondrial HMG-CoA synthase, involved in cholesterol synthesis. The complementary strategies of 2-DE coupled either with database spot mapping or protein isolation and amino acid sequencing successfully identified a subset of proteins from xenobiotic-damaged rodent livers, the expression of which differed from controls. However, the current bio-informatics platform for rodent hepatic proteins and limited knowledge of specific protein functionality restricted application of this **proteomics** profile to further define a mechanistic basis for this unusual hepatotoxicity.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:609661 CAPLUS
DOCUMENT NUMBER: 133:292958
TITLE: **Proteomics**: applications in basic and applied biology
AUTHOR(S): **Anderson, N. Leigh;** Matheson, Alastair D.; **Steiner, Sandra**
CORPORATE SOURCE: Large Scale Proteomics Corporation, Rockville, MD, 20850, USA
SOURCE: Current Opinion in Biotechnology (2000), 11(4), 408-412
CODEN: CUOBE3; ISSN: 0958-1669
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 37 refs. The rapid evolution of **proteomics** has continued during the past year, with a series of innovations in the core technologies of two-dimensional electrophoresis and mass spectrometry, and a diversity of productive research programs. Well-annotated **proteomics** databases are now emerging in a no. of fields to provide a platform for systematic research, with particularly promising progress in clin. applications such as cardiol. and oncol. Large-scale quant. research, comparable in power and sensitivity to that achieved for

gene expression, is thus becoming a reality at the protein level.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 10 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998287948 EMBASE
TITLE: New insights into cyclosporine A nephrotoxicity by **proteome** analysis.
AUTHOR: Aicher L.; Wahl D.; Arce A.; Grenet O.; **Steiner S.**
CORPORATE SOURCE: Dr. S. Steiner, Preclinical Safety, Toxicology/Pathology, Novartis Pharma AG, WS-2881, CH-4002 Basel, Switzerland. sandra.steiner@pharma.novartis.com
SOURCE: Electrophoresis, (1998) 19/11 (1998-2003). Refs: 11
ISSN: 0173-0835 CODEN: ELCTDN
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
028 Urology and Nephrology
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Using two-dimensional gel electrophoresis (2-DE), we recently discovered an association between decreased calcium-binding protein, calbindin-D 28 kDa, urinary calcium wasting and intratubular corticomedullary calcifications in rat kidney. This observation prompted us to investigate kidney tissues of other species, including man. In this paper we show that in dogs and monkeys, which are generally devoid of cyclosporine A (CsA)-mediated nephrotoxicity, renal calbindin levels were not affected by the CsA treatment whereas in CsA- treated human kidney-transplant recipients with renal vascular or tubular toxicity, a marked decrease in renal calbindin-D 28 kDa protein level was found in most of the kidney biopsy sections. The present results strongly suggest that calbindin is a marker for CsA-nephrotoxicity. The discovery of calbindin-D 28 kDa being involved in CsA toxicity has evolved from the application of 2-DE and has not been reported previously, proving that **proteomics** can provide essential information in mechanistic toxicology. Considering the current improvements in **proteome** methods it is expected that high throughput **proteomics** will become an indispensable tool in preclinical safety testing.

L150 ANSWER 11 OF 12 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-304421 [34] WPIDS
DOC. NO. NON-CPI: N2002-238158
DOC. NO. CPI: C2002-088615
TITLE: Computer-readable structure, useful for organizing database elements corresponding to proteins in tissue obtained from organism, comprises records, parameter field, location field and abundance field.
DERWENT CLASS: B04 C07 D16 S03 T04
INVENTOR(S): **ANDERSON, N G; ANDERSON, N L; ANDERSON, N**
PATENT ASSIGNEE(S): (ANDE-I) ANDERSON N G; (ANDE-I) ANDERSON N L; (LARG-N) LARGE SCALE PROTEOMICS CORP
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002021428	A1	20020314	(200234)*	EN	93

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2002028005 A1 20020307 (200234)
US 2002087273 A1 20020704 (200247)
AU 2001088501 A 20020322 (200251)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002021428	A1	WO 2001-US26933	20010831
US 2002028005	A1 CIP of	US 2000-654133	20000901
		US 2001-753678	20010104
US 2002087273	A1 CIP of	US 2001-753678	20010104
		US 2001-756285	20010109
AU 2001088501	A	AU 2001-88501	20010831

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001088501	A Based on	WO 200221428

PRIORITY APPLN. INFO: US 2001-756285 20010109; US 2000-654133 20000901; US 2001-753678 20010104

AB WO 200221428 A UPAB: 20020528

NOVELTY - A computer-readable structure comprising records for storing different types of data relating to respective proteins, a parameter field for indicating a selected characteristic of the corresponding protein, a location field for indicating the relative location in the organism from which the protein was obtained, and an abundance field for indicating the relative amount of the protein, is new.

DETAILED DESCRIPTION - A computer-readable structure, encoded on a computer-readable medium, comprises records for storing different types of data relating to respective proteins, a parameter field for indicating a selected characteristic of the corresponding protein, a location field for indicating the relative location in the organism from which the corresponding protein was obtained, and an abundance field for indicating the relative amount of the corresponding protein obtained from the location, where each record has at least an identification field for identifying a corresponding one of the proteins, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a computer program product for extracting selected data relating to a protein from a database comprising a computer-readable medium, a user interface module for guiding a user to generate at least one query to retrieve selected data from the database, a database search module communicatively coupled to the user interface module and operable to locate and retrieve the database that correspond to the query;

(2) determining the **proteome** of an individual comprising taking a protein containing sample from each of at least 5 tissue from an individual and determining the presence and relative abundance of at least 10 proteins from each of the tissues;

(3) identifying a protein marker that indicates a condition by change in abundance comprising determining the abundance of a candidate protein marker in the same biological samples that have different selected characteristic(s), accessing a database comprising entries for providing data relating to proteins including the candidate protein marker, and comparing the abundance of the candidate protein marker to the entries in the database;

(4) obtaining **proteomic** information comprising generating a query to retrieve selected data relating to a protein from the computer

program, locating a record in the protein index database that satisfies protein characteristics requested via the query and generating an output corresponding to the record;

(5) identifying component-specific proteins from a database comprising information relating to a number of proteins comprising:

(a) generating a first list of all proteins indicated in the database as being located in a specimen of a first selected component;

(b) generating a second list of all proteins indicated in the database as being located in a specimen of a second selected component;

(c) subtracting from the first list all of the proteins common to both lists; and

(d) repeating steps (b) and (c) for components 3-n, where n is the total number of components in the database;

(6) creating a polypeptide database comprising:

(a) generating a 2-D separation of polypeptides of two sources;

(b) generating an electronic image of the 2-D separation of polypeptides of the two sources;

(c) warping one of the electronic images of the 2-D separation of polypeptides to the other image;

(d) analyzing the two 2-D separation of polypeptides of the sources to determine polypeptide spots common to both tissues;

(e) confirming commonality of at least a portion of the polypeptide spots common in both the two 2-D separation of polypeptides;

(f) recording in a database polypeptide spots common to both tissues as being the same in response to positive confirmation of the portion of the spots common to both 2D separation of polypeptides;

(g) analyzing polypeptide spots not common to both 2-D separations; and

(h) recording in the database results of the analyzing the polypeptide spots not common to both 2-D separations;

(7) identifying a polypeptide in a sample from an individual of a randomly breeding population comprising:

(a) characterizing the polypeptide by isoelectric point and molecular weight;

(b) identifying tissues of the subject where the polypeptide is found to yield distinguishing parameters of the polypeptide comprising isoelectric point, molecular weight and tissue distribution;

(c) comparing parameters with distinguishing parameters of previously tested polypeptides of a set; and

(d) determining whether a previously tested polypeptide has the parameters of the polypeptide; and

(8) a data processing system for determining identity of an element (N+1) to N elements of a database contained in a storage medium comprising computer processing mechanism, data storage mechanism, and mechanism for processing data regarding comparing a parameter of the (N+1) element with the parameter of the N elements of the database, where:

(a) the element is a protein or polypeptide;

(b) processing data is repeated at least M times, where each M parameter is examined at each iteration (where M is at least 3) and when the (N+1) element does not have M identical parameters of N element(s), the data storage mechanism adds data of the (N+1) element and of the M parameters to the database to produce a new database comprising (N+1) elements;

(c) the database comprises database elements corresponding to proteins in tissues obtained from a selected organism; and

(d) a difference in abundance of the candidate protein marker identifies the candidate protein marker as a protein marker for the condition.

USE - For organizing database elements corresponding to proteins in tissue obtained from a selected organism, organelle, cell, tissue, organ, or population.

ADVANTAGE - The invention can measure the same protein in multiple different tissues. It can also measure the abundance of a protein at a

particular location.

DESCRIPTION OF DRAWING(S) - The figure is a schematic block diagram showing the steps that form part of the analysis for comparing proteins of different tissues.

Dwg.1/9

L150 ANSWER 12 OF 12 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-351264 [38] WPIDS
CROSS REFERENCE: 2001-648040 [74]; 2002-215479 [27]; 2002-635199 [68]
DOC. NO. NON-CPI: N2002-276053
DOC. NO. CPI: C2002-099670
TITLE: Liquid density gradient production method for molecular biology field, involves supplying specified liquid into vessel, such that it contacts surface of float on entering the vessel to form separate layer above other liquid.
DERWENT CLASS: A88 P41
INVENTOR(S): **ANDERSON, N G**
PATENT ASSIGNEE(S): (ANDE-I) ANDERSON N G
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002042335	A1	20020411	(200238)*		15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002042335	A1 CIP of	US 2000-551314	20000418
		US 2001-836344	20010418

PRIORITY APPLN. INFO: US 2001-836344 20010418; US 2000-551314 20000418

AB US2002042335 A UPAB: 20021026

NOVELTY - A float is inserted in a vessel into which two liquid are supplied. One of the liquid, is fed to the vessel such that it contacts the surface of the float on entering the vessel, to form a separate layer above the other liquid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(a) Liquid density gradient producing apparatus;

(b) Float;

(c) Nucleated cells isolating apparatus; and

(d) Isolation method of nucleated cells from blood.

USE - In molecular biology field for rate-zonal separations, isopycnic banding separations, for separation of nucleated cells from blood. Is also used in **proteomics** research.

ADVANTAGE - Enables forming multiplicity of liquid density gradients in vessels, simply and effectively.

DESCRIPTION OF DRAWING(S) - The figure shows a side view of vessel and float to produce liquid density gradient in the vessel.

Dwg.1F/5

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=> fil capl
FILE 'CAPLUS' )ENTERED AT 15:19:33 ON 13 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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text search

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FILE COVERS 1907 - 13 Feb 2003  VOL 138 ISS 7
FILE LAST UPDATED: 12 Feb 2003  (20030212/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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L11       45108 SEA FILE=CAPLUS ABB=ON  MARKER#/OBI
L13       76368 SEA FILE=CAPLUS ABB=ON  TARGET?/OBI
L14         343 SEA FILE=CAPLUS ABB=ON  L7 AND PHARMAC?/SC,SX
L15         218 SEA FILE=CAPLUS ABB=ON  L7 AND (L11 OR L13)
L16          68 SEA FILE=CAPLUS ABB=ON  L14 AND L15
L17      609728 SEA FILE=CAPLUS ABB=ON  PROTEINS/CT
L18       41221 SEA FILE=CAPLUS ABB=ON  L17(L)(ANST OR DGN)/RL
L20       22543 SEA FILE=CAPLUS ABB=ON  DRUG SCREENING+OLD/CT
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L23       35932 SEA FILE=CAPLUS ABB=ON  HYPERTENSION/CT
L24       14949 SEA FILE=CAPLUS ABB=ON  OBESITY/CT
L25        1785 SEA FILE=CAPLUS ABB=ON  OSTEOARTHRITIS/CT
L26        7960 SEA FILE=CAPLUS ABB=ON  OSTEOPOROSIS/CT
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L29        3261 SEA FILE=CAPLUS ABB=ON  ANTIOBESITY AGENTS+OLD/CT
L30        4524 SEA FILE=CAPLUS ABB=ON  ANTIARTHRITICS+OLD/CT
L38       15439 SEA FILE=CAPLUS ABB=ON  METABOLIC(2A)PATHWAY#
L39           9 SEA FILE=CAPLUS ABB=ON  L16 AND L18 AND (L20 OR (L22 OR L23 OR
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- Role ANST- analytical study
DGN - diagnostic use

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L30        4524 SEA FILE=CAPLUS ABB=ON  ANTIARTHRITICS+OLD/CT
L38       15439 SEA FILE=CAPLUS ABB=ON  METABOLIC(2A)PATHWAY#
L40           6 SEA FILE=CAPLUS ABB=ON  L16 AND L20 AND ((L22 OR L23 OR L24 OR
                L25 OR L26 OR L27 OR L28 OR L29 OR L30) OR L38)


L7         4153 SEA FILE=CAPLUS ABB=ON  PROTEOM?
L11       45108 SEA FILE=CAPLUS ABB=ON  MARKER#/OBI
L13       76368 SEA FILE=CAPLUS ABB=ON  TARGET?/OBI
L14         343 SEA FILE=CAPLUS ABB=ON  L7 AND PHARMAC?/SC,SX
L15         218 SEA FILE=CAPLUS ABB=ON  L7 AND (L11 OR L13)
L43        5591 SEA FILE=CAPLUS ABB=ON  METABOLIC(2A)PATHWAY#/OBI
L44           2 SEA FILE=CAPLUS ABB=ON  (L14 OR L15) AND L43


=> s (139 or 140 or 144) not 1149

L151         11 (L39 OR L40 OR L44) NOT L149
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previously printed w/ inventor search

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=> fil medl

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 FILE LAST UPDATED: 12 FEB 2003 (20030212/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que 166; d que 170; d que 176;d que 163

L50        3026 SEA FILE=MEDLINE ABB=ON  PROTEOM?
L55       50163 SEA FILE=MEDLINE ABB=ON  OBESITY+NT/CT
L56       20416 SEA FILE=MEDLINE ABB=ON  OSTEOPOROSIS+NT/CT
L57      155298 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS+NT/CT
L58       21719 SEA FILE=MEDLINE ABB=ON  OSTEOARTHRITIS+NT/CT
L59      156353 SEA FILE=MEDLINE ABB=ON  HYPERTENSION+NT/CT
L65       51696 SEA FILE=MEDLINE ABB=ON  (L55 OR L56 OR L57 OR L58 OR L59)(L)(G
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– Subheadings GE - genetics DI - diagnosis

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L50        3026 SEA FILE=MEDLINE ABB=ON  PROTEOM?
L67      444612 SEA FILE=MEDLINE ABB=ON  TARGET? OR MARKER#
L68        6952 SEA FILE=MEDLINE ABB=ON  METABOLIC PATHWAY#
L70           5 SEA FILE=MEDLINE ABB=ON  L50 AND L68 AND L67


L50        3026 SEA FILE=MEDLINE ABB=ON  PROTEOM?
L51       71919 SEA FILE=MEDLINE ABB=ON  DRUG EVALUATION, PRECLINICAL+NT/CT
L52        8646 SEA FILE=MEDLINE ABB=ON  DRUG DESIGN/CT
L67      444612 SEA FILE=MEDLINE ABB=ON  TARGET? OR MARKER#
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L74        1357 SEA FILE=MEDLINE ABB=ON  PHARMACOGENETICS/CT
L76           3 SEA FILE=MEDLINE ABB=ON  L50 AND (L51 OR L52) AND L67 AND L74


L50        3026 SEA FILE=MEDLINE ABB=ON  PROTEOM?
L51       71919 SEA FILE=MEDLINE ABB=ON  DRUG EVALUATION, PRECLINICAL+NT/CT
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L54         101 SEA FILE=MEDLINE ABB=ON  L50 AND (L51 OR L52)
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L57      155298 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS+NT/CT
L58       21719 SEA FILE=MEDLINE ABB=ON  OSTEOARTHRITIS+NT/CT
L59      156353 SEA FILE=MEDLINE ABB=ON  HYPERTENSION+NT/CT
L60       26213 SEA FILE=MEDLINE ABB=ON  ANTIHYPERTENSIVE AGENTS/CT
L61         430 SEA FILE=MEDLINE ABB=ON  ANTI-OBESITY AGENTS/CT
L62       11797 SEA FILE=MEDLINE ABB=ON  HYPOGLYCEMIC AGENTS/CT
L63           0 SEA FILE=MEDLINE ABB=ON  L54 AND (L55 OR L56 OR L57 OR L58 OR
                L59 OR L60 OR L61 OR L62)


=> s (l66 or l70 or l76) not l53

L152         14 (L66 OR L70 OR L76) NOT L53

=> fil embase

FILE 'EMBASE' ENTERED AT 15:19:38 ON 13 FEB 2003
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 FILE COVERS 1974 TO 7 Feb 2003 (20030207/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d que l106; d que l112; d que l115; d que l118

L85        2659 SEA FILE=EMBASE ABB=ON  PROTEOM?
L87       61966 SEA FILE=EMBASE ABB=ON  DRUG SCREENING/CT
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L89        7161 SEA FILE=EMBASE ABB=ON  DISEASE MARKER/CT
L90       18616 SEA FILE=EMBASE ABB=ON  DRUG TARGETING+NT/CT
L101     177100 SEA FILE=EMBASE ABB=ON  DRUG DEVELOPMENT/CT
L106          8 SEA FILE=EMBASE ABB=ON  L85 AND L89 AND (L87 OR L88 OR L90 OR
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L89        7161 SEA FILE=EMBASE ABB=ON  DISEASE MARKER/CT
L91       45089 SEA FILE=EMBASE ABB=ON  OBESITY+NT/CT
L92       24687 SEA FILE=EMBASE ABB=ON  OSTEOPOROSIS+NT/CT
L93      142687 SEA FILE=EMBASE ABB=ON  DIABETES MELLITUS+NT/CT
L94       13320 SEA FILE=EMBASE ABB=ON  OSTEOARTHRITIS+NT/CT
L95      164369 SEA FILE=EMBASE ABB=ON  HYPERTENSION+NT/CT
L96       18623 SEA FILE=EMBASE ABB=ON  ANTIHYPERTENSIVE AGENT/CT
L97         347 SEA FILE=EMBASE ABB=ON  ANTIOBESITY AGENT/CT
L98        4867 SEA FILE=EMBASE ABB=ON  ANTIDIABETIC AGENT/CT
L99           1 SEA FILE=EMBASE ABB=ON  ANTIOSTEOPOROTIC AGENT/CT
L111      36178 SEA FILE=EMBASE ABB=ON  METABOLISM/CT
L112          2 SEA FILE=EMBASE ABB=ON  L85 AND L89 AND ((L91 OR L92 OR L93 OR
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previously printed

L94 OR L95 OR L96 OR L97 OR L98 OR L99) OR L111)

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L92	24687	SEA FILE=EMBASE ABB=ON	OSTEOPOROSIS+NT/CT
L93	142687	SEA FILE=EMBASE ABB=ON	DIABETES MELLITUS+NT/CT
L94	13320	SEA FILE=EMBASE ABB=ON	OSTEOARTHRITIS+NT/CT
L95	164369	SEA FILE=EMBASE ABB=ON	HYPERTENSION+NT/CT
L96	18623	SEA FILE=EMBASE ABB=ON	ANTIHYPERTENSIVE AGENT/CT
L97	347	SEA FILE=EMBASE ABB=ON	ANTIOBESITY AGENT/CT
L98	4867	SEA FILE=EMBASE ABB=ON	ANTIDIABETIC AGENT/CT
L99	1	SEA FILE=EMBASE ABB=ON	ANTIOSTEOPOROTIC AGENT/CT
L101	177100	SEA FILE=EMBASE ABB=ON	DRUG DEVELOPMENT/CT
L111	36178	SEA FILE=EMBASE ABB=ON	METABOLISM/CT
L114	206349	SEA FILE=EMBASE ABB=ON	L87/MAJ OR L88/MAJ OR L90/MAJ OR L101/MAJ
L115	5	SEA FILE=EMBASE ABB=ON	L85 AND ((L91 OR L92 OR L93 OR L94 OR L95 OR L96 OR L97 OR L98 OR L99) OR L111) AND L114

L85	2659	SEA FILE=EMBASE ABB=ON	PROTEOM?
L87	61966	SEA FILE=EMBASE ABB=ON	DRUG SCREENING/CT
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L90	18616	SEA FILE=EMBASE ABB=ON	DRUG TARGETING+NT/CT
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L94	13320	SEA FILE=EMBASE ABB=ON	OSTEOARTHRITIS+NT/CT
L95	164369	SEA FILE=EMBASE ABB=ON	HYPERTENSION+NT/CT
L96	18623	SEA FILE=EMBASE ABB=ON	ANTIHYPERTENSIVE AGENT/CT
L97	347	SEA FILE=EMBASE ABB=ON	ANTIOBESITY AGENT/CT
L98	4867	SEA FILE=EMBASE ABB=ON	ANTIDIABETIC AGENT/CT
L99	1	SEA FILE=EMBASE ABB=ON	ANTIOSTEOPOROTIC AGENT/CT
L101	177100	SEA FILE=EMBASE ABB=ON	DRUG DEVELOPMENT/CT
L111	36178	SEA FILE=EMBASE ABB=ON	METABOLISM/CT
L116	241	SEA FILE=EMBASE ABB=ON	L85 AND (L87 OR L88 OR L90 OR L101)
L118	2	SEA FILE=EMBASE ABB=ON	L116 AND (L91/MAJ OR L92/MAJ OR L93/MAJ OR L94/MAJ OR L95/MAJ OR L96/MAJ OR L97/MAJ OR L98/MAJ OR L99 OR L111/MAJ)

=> s (l106 or l112 or l115 or l118) not l100

L153 15 (L106 OR L112 OR L115 OR L118) NOT L100

=> fil wpids; d que l135; d que l136; d que l147

FILE 'WPIDS' ENTERED AT 15:19:40 ON 13 FEB 2003
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FILE LAST UPDATED: 11 FEB 2003 <20030211/UP>
MOST RECENT DERWENT UPDATE: 200310 <200310/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> DUE TO TECHNICAL ISSUES THE SDIS FOR UPDATES 200302-200304
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>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

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L124        276 SEA FILE=WPIDS ABB=ON  PROTEOM?
L132        484 SEA FILE=WPIDS ABB=ON  METABOLIC PATHWAY#
L134      57520 SEA FILE=WPIDS ABB=ON  DRUG#
L135          2 SEA FILE=WPIDS ABB=ON  L124 AND L132 AND L124 AND L134


L124        276 SEA FILE=WPIDS ABB=ON  PROTEOM?
L125     140493 SEA FILE=WPIDS ABB=ON  MARKER# OR TARGET?
L127      22275 SEA FILE=WPIDS ABB=ON  ?DIABET?
L128       6607 SEA FILE=WPIDS ABB=ON  ?OSTEOPORO?
L129      19126 SEA FILE=WPIDS ABB=ON  ?OSTEOARTHRI? OR ?ARTHRITI?
L130       5581 SEA FILE=WPIDS ABB=ON  OBESITY OR ANTIOBESITY
L131      17813 SEA FILE=WPIDS ABB=ON  ?HYPERTENS?
L132        484 SEA FILE=WPIDS ABB=ON  METABOLIC PATHWAY#
L134      57520 SEA FILE=WPIDS ABB=ON  DRUG#
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L124        276 SEA FILE=WPIDS ABB=ON  PROTEOM?
L125     140493 SEA FILE=WPIDS ABB=ON  MARKER# OR TARGET?
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L128       6607 SEA FILE=WPIDS ABB=ON  ?OSTEOPORO?
L129      19126 SEA FILE=WPIDS ABB=ON  ?OSTEOARTHRI? OR ?ARTHRITI?
L130       5581 SEA FILE=WPIDS ABB=ON  OBESITY OR ANTIOBESITY
L131      17813 SEA FILE=WPIDS ABB=ON  ?HYPERTENS?
L132        484 SEA FILE=WPIDS ABB=ON  METABOLIC PATHWAY#
L134      57520 SEA FILE=WPIDS ABB=ON  DRUG#
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L142         58 SEA FILE=WPIDS ABB=ON  (L137 OR L134)(5A)L125 (L) L124
L147          9 SEA FILE=WPIDS ABB=ON  L142(L)(L127 OR L128 OR L129 OR L130 OR
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=> s (l135 or l136 or l147) not l126

L154          9 (L135 OR L136 OR L147) NOT (L126)
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previously printed

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FILE 'CAPLUS' ENTERED AT 15:20:01 ON 13 FEB 2003
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FILE 'WPIDS' ENTERED AT 15:20:01 ON 13 FEB 2003

PROCESSING COMPLETED FOR L152
PROCESSING COMPLETED FOR L151
PROCESSING COMPLETED FOR L153
PROCESSING COMPLETED FOR L154
L155 49 DUP REM L152 L151 L153 L154 (0 DUPLICATES REMOVED)
ANSWERS '1-14' FROM FILE MEDLINE
ANSWERS '15-25' FROM FILE CAPLUS
ANSWERS '26-40' FROM FILE EMBASE
ANSWERS '41-49' FROM FILE WPIDS

=> d ibib ab 1-49; fil hom

L155 ANSWER 1 OF 49 MEDLINE
ACCESSION NUMBER: 2002182327 MEDLINE
DOCUMENT NUMBER: 21912611 PubMed ID: 11914111
TITLE: Placental peptides as markers of gestational disease.
AUTHOR: Page Nigel M; Kemp C Fred; Butlin David J; Lowry Philip J
CORPORATE SOURCE: School of Animal and Microbial Sciences, The University of Reading, RG6 6AJ, UK.. sasnpage@reading.ac.uk
SOURCE: Reproduction, (2002 Apr) 123 (4) 487-95. Ref: 73
Journal code: 100966036. ISSN: 1470-1626.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020401
Last Updated on STN: 20020814
Entered Medline: 20020813

AB The human placenta produces a wide range of important peptides, of which an intricate balance is required throughout pregnancy. In a gestational disease, this balance may be disturbed and the identification of such changes may be used to detect a particular pathology or to ascertain its severity. This review considers the role and association of various placental peptide markers associated with the major gestational diseases including intrauterine growth retardation, pre-term labour, pre-eclampsia, chromosomal disorders, gestational diabetes and trophoblastic disease. Potential markers that may prove more reliable and specific in their diagnostic value and that may be used for identifying patients at risk are also discussed. The importance of the new fields of genomics and **proteomics** in the future discovery of new peptide markers is illustrated.

L155 ANSWER 2 OF 49 MEDLINE
ACCESSION NUMBER: 2002464233 IN-PROCESS
DOCUMENT NUMBER: 22211605 PubMed ID: 12223073
TITLE: Functional genomics in neuropsychiatric disorders and in neuropharmacology.
AUTHOR: Castren Eero; Kontkanen Outi
CORPORATE SOURCE: Department of Neurobiology, A.I. Virtanen Institute and Department of Psychiatry, University of Kuopio, PO Box 1627, 70211 Kuopio, Finland.. Eero.Castren@uku.fi

SOURCE: Expert Opin Ther Targets, (2002 Jun) 6 (3) 363-74.
Journal code: 101127833. ISSN: 1472-8222.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020912
Last Updated on STN: 20021213

AB The rapidly accumulating amount of information concerning gene and protein expression patterns produced by functional genomics, **proteomics** and bioinformatics is presently providing new **targets** for drug development. Furthermore, the analysis of gene expression in cells and tissues affected by a disease may reveal the underlying **metabolic pathways** and cellular processes affected. Finally, changes in gene expression may be used in either diagnostics or the monitoring of drug responses. This review focuses on advances in the use of functional genomics in neurological and neuropsychiatric diseases and neuropsychopharmacology. Although the number of published studies in this field is still limited, it already appears that this strategy may become a fruitful means in the analysis of the aetiology of neuropsychiatric disorders and the search for novel neuropharmacological drugs.

L155 ANSWER 3 OF 49 MEDLINE
ACCESSION NUMBER: 2002485628 MEDLINE
DOCUMENT NUMBER: 22232738 PubMed ID: 12271509
TITLE: Pharmacogenomics: the frontiers of genome medicine.
AUTHOR: Tanaka Toshio; Tsujimoto Gozoh; Sugiyama Yuichi; Hashimoto Yasuhiro
CORPORATE SOURCE: Molecular and Cellular Pharmacology, Mie University School of Medicine, Tsu, Mie 514-8507, Japan.
SOURCE: NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (2002 Sep) 120 (3) 141-8. Ref: 20
Journal code: 0420550. ISSN: 0015-5691.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020926
Last Updated on STN: 20021217
Entered Medline: 20021204

AB The Human Genome Project provides insights so profound that it has the ability to change everything we know about medicine and how medicines are developed. Pharmacogenomics is defined as studies to identify the genes that are involved in determining the responsiveness to a given drug and to distinguish responders and non-responders to a given drug. Genome sequencing, transcriptome, and **proteome** analysis are of particular significance in pharmacogenomics. Transcriptome analysis can be done by methods of random cDNA sequencing, mRNA display and, differential hybridization (i.e., cDNA microarray and associated methods). Our results suggest that the pharmacogenomic transcriptome analysis and pharmainformatics have potential as strategies for defining novel drug **targets** in various diseases. Pharmacogenomics enhances the development, commercialization, and clinical use of conventional pharmaceutical products for common diseases, and it will eventually become a powerful tool for Evidence-Based Medicine. It is also important to predict interindividual pharmacokinetic differences by genetic polymorphisms of transporters or pharmacokinetic changes by transporter-mediated drug interactions during drug development. Pharmacogenomics and pharmainformatics enable us to move quickly and efficiently from **targets** to appropriate medicines.

L155 ANSWER 4 OF 49 MEDLINE
ACCESSION NUMBER: 2002108487 MEDLINE
DOCUMENT NUMBER: 21829487 PubMed ID: 11839187
TITLE: **Metabolic pathway** analysis in trypanosomes and malaria parasites.
AUTHOR: Fairlamb Alan H
CORPORATE SOURCE: Division of Biological Chemistry and Molecular Microbiology, The Wellcome Trust Biocentre, University of Dundee, Dundee DD1 5EH, UK.. a.h.fairlamb@dundee.ac.uk
SOURCE: PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON. SERIES B: BIOLOGICAL SCIENCES, (2002 Jan 29) 357 (1417) 101-7. Ref: 40
Journal code: 7503623. ISSN: 0962-8436.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020213
Last Updated on STN: 20020713
Entered Medline: 20020712

AB Identification of novel drug **targets** is required for the development of new classes of drugs to overcome drug resistance and replace less efficacious treatments. In theory, knowledge of the entire genome of a pathogen identifies every potential drug **target** in any given microbe. In practice, the sheer complexity and the inadequate or inaccurate annotation of genomic information makes **target** identification and selection somewhat more difficult. Analysis of **metabolic pathways** provides a useful conceptual framework for the identification of potential drug **targets** and also for improving our understanding of microbial responses to nutritional, chemical and other environmental stresses. A number of metabolic databases are available as tools for such analyses. The strengths and weaknesses of this approach are discussed.

L155 ANSWER 5 OF 49 MEDLINE
ACCESSION NUMBER: 2002367627 MEDLINE
DOCUMENT NUMBER: 22108855 PubMed ID: 12116177
TITLE: Combined genome and **proteome** approach to identify new susceptibility genes.
AUTHOR: Pociot Flemming; Karlsen Allan E
CORPORATE SOURCE: Steno Diabetes Center, Gentofte, Denmark.. fpoc@novo.dk
CONTRACT NUMBER: DK-96-012 (NIDDK)
SOURCE: AMERICAN JOURNAL OF MEDICAL GENETICS, (2002 May 30) 115 (1) 55-60. Ref: 27
Journal code: 7708900. ISSN: 0148-7299.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020713
Last Updated on STN: 20030129
Entered Medline: 20030128

AB Type 1 diabetes mellitus (T1DM) is a multifactorial disorder characterized by a specific destruction of the insulin-producing beta cells in the islets of Langerhans. Cells from the immune system infiltrate the islet during the pathogenesis, releasing a mixture of cytokines demonstrated to

be specifically toxic to the beta cells within the islets. The goal is to understand the molecular mechanisms responsible for this specific beta-cell toxicity, which will allow the design of novel intervention strategies for T1DM. The **proteome** approach provides a detailed picture of the beta-cell proteins changing expression pattern during cytokine-mediated beta-cell destruction. Combining the information from this **proteome** approach with genetic studies makes us believe that it is possible to reach this goal.

L155 ANSWER 6 OF 49 MEDLINE
ACCESSION NUMBER: 2002082048 MEDLINE
DOCUMENT NUMBER: 21667499 PubMed ID: 11808338
TITLE: Pharmacogenomics and pharmainformatics.
AUTHOR: Tanaka Toshio; Nishimura Yuhei; Tsunoda Hiroshi; Kitaoka Yoshikuni; Naka Michiko
CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, Mie University School of Medicine.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2002 Jan) 60 (1) 39-50. Ref: 19
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020128
Last Updated on STN: 20020227
Entered Medline: 20020226

AB Pharmacogenomics is defined to identify the genes which are involved in determining the responsiveness and to distinguish responders and non-responders to a given drug. Genome sequencing, transcriptome and **proteome** analysis are of particular significance in pharmacogenomics. Sequencing is used to locate polymorphisms, and monitoring of gene expression can provide clue about the genomic response to disease and treatment. The transcriptome analysis can be done by methods of random cDNA sequencing (expressed sequence tag project, body map project, serial analysis of gene expression, et al), mRNA display (differential display, fluorescent differential display, RNA arbitraly primed PCR, molecular indexing, gene expression fingerprinting, et al) and differential hybridization(cDNA high density filter, cDNA microarray, oligomicrochip, et al). We used transcriptome analysis to identify therapeutic **target** genes by studying change of gene expression in animal models of cerebral vasospasm (1) and of hypoxia/ischemia and found novel drug **target** candidates through this pharmacogenomic strategy (2). We found remarkable up-regulation of heme oxygenase-1(HO-1) mRNA in the basilar artery and it might be closely related to the occurrence of delayed vasospasm after subarachnoid hemorrhage. In this report, we clearly demonstrate that intrathecal administration of antisense HO-1 oligodeoxynucleotide aggravates vasospasm, suggesting HO-1 gene induction has spasmolytic effects. Furthermore, we found the protective effects of HO-1 gene induction by endogenous or clinical compounds in cerebral vasospasm. Therapeutic gene induction of HO-1 could be a novel strategy for the prevention and treatment of Hb-induced pathologic conditions including delayed cerebral vasospasm. Our results suggest that the pharmacogenomic transcriptome analysis and pharmainformatics has the potential for strategy to define novel drug **targets** in various diseases (3). (1) J Clin Invest 104: 59-66, 1999. (2) J Biol Chem 276: 19921-19928, 2001. (3) J Cardiovasc Pharm 36: S1-S4, 2000.

L155 ANSWER 7 OF 49 MEDLINE
ACCESSION NUMBER: 2001400925 MEDLINE
DOCUMENT NUMBER: 21345483 PubMed ID: 11451470
TITLE: Industrial-scale, genomics-based drug design and discovery.
AUTHOR: Dean P M; Zanders E D; Bailey D S
CORPORATE SOURCE: De Novo Pharmaceuticals Ltd, St Andrew's House, 59 St Andrew's Street, CB2 3DD., Cambridge, UK.. philip.dean@denovopharma.com
SOURCE: TRENDS IN BIOTECHNOLOGY, (2001 Aug) 19 (8) 288-92. Journal code: 8310903. ISSN: 0167-7799.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB The demands on drug discovery organizations have increased dramatically in recent years, partly because of the need to identify novel **targets** that are both relevant to disease and chemically tractable. This is leading to an industrial approach to traditional biology and chemistry, inspired in part by the revolution in genomics. The purpose of this article is to highlight the flow of investigation from gene sequence of potential therapeutic **targets**, through mRNA and protein expression, to protein structure and drug design. To deal with this scale of activity, many commercial and public organizations have been established and some of the key players will be listed in this article.

L155 ANSWER 8 OF 49 MEDLINE
ACCESSION NUMBER: 2002064268 MEDLINE
DOCUMENT NUMBER: 21650501 PubMed ID: 11790888
TITLE: **Proteome** analysis--a novel approach to understand the pathogenesis of Type 1 diabetes mellitus.
AUTHOR: Karlsen A E; Sparre T; Nielsen K; Nerup J; Pociot F
CORPORATE SOURCE: Steno Diabetes Center, Niels Steensensvej 2, DK-2820 Gentofte, Denmark.
SOURCE: DISEASE MARKERS, (2001) 17 (4) 205-16. Journal code: 8604127. ISSN: 0278-0240.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020130
Entered Medline: 20020129

AB Type 1 (insulin-dependent) diabetes mellitus (T1DM) is associated with a specific destruction of the insulin-producing beta-cells in the islets of Langerhans. Several factors, e.g. genetic, environmental and immunologial, may be involved in the etiology and pathogenesis of T1DM. Autoreactive T- and B-lymphocytes, together with macrophages infiltrate the islets during the pathogenesis, releasing a mixture of cytokines, demonstrated to be specifically toxic to the beta-cells within the islets. Our goal is to understand the molecular mechanisms responsible for the beta-cell specific toxicity enabling us to design novel intervention strategies in T1DM. The **proteome** approach allows us to get a detailed picture of the beta-cell proteins, which change expression level or are post-translationally modified in different in vitro and in vivo models of T1DM-associated beta-cell destruction. Combining the information obtained from this extended **proteome** approach, with that of genetic-, transcriptome- and candidate-gene approaches, we believe that it is possible to reach this goal.

L155 ANSWER 9 OF 49 MEDLINE
ACCESSION NUMBER: 2001573766 MEDLINE
DOCUMENT NUMBER: 21537963 PubMed ID: 11680894
TITLE: The mouse SWISS-2D PAGE database: a tool for **proteomics** study of diabetes and obesity.
AUTHOR: Sanchez J C; Chiappe D; Converset V; Hoogland C; Binz P A; Paesano S; Appel R D; Wang S; Sennitt M; Nolan A; Cawthorne M A; Hochstrasser D F
CORPORATE SOURCE: Clinical Chemistry Laboratory, University Hospital, Geneva, Switzerland.. sanchez@dim.hcuge.ch
SOURCE: Proteomics, (2001 Jan) 1 (1) 136-63.
Journal code: 101092707. ISSN: 1615-9853.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011030
Last Updated on STN: 20020123
Entered Medline: 20011218

AB A number of two-dimensional electrophoresis (2-DE) reference maps from mouse samples have been established and could be accessed through the internet. An up-to-date list can be found in WORLD-2D PAGE (http://www.expasy.ch/ch2d/2d- index.html), an index of 2-DE databases and services. None of them were established from mouse white and brown adipose tissues, pancreatic islets, liver nuclei and skeletal muscle. This publication describes the mouse SWISS-2D PAGE database. Proteins present in samples of mouse (C57BI/6J) liver, liver nuclei, muscle, white and brown adipose tissue and pancreatic islets are assembled and described in an accessible uniform format. SWISS-2D PAGE can be accessed through the World Wide Web (WWW) network on the ExPASy molecular biology server (http://www.expasy.ch/ ch2d/).

L155 ANSWER 10 OF 49 MEDLINE
ACCESSION NUMBER: 2001682038 MEDLINE
DOCUMENT NUMBER: 21584520 PubMed ID: 11728000
TITLE: Applications of yeast in drug discovery.
AUTHOR: Ma D
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285, USA.. ma_doreen@lilly.com
SOURCE: PROGRESS IN DRUG RESEARCH, (2001) 57 117-62. Ref: 161
Journal code: 1304021. ISSN: 0071-786X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011203
Last Updated on STN: 20020130
Entered Medline: 20020129

AB The yeast Saccharomyces cerevisiae is perhaps the best-studied eukaryotic organism. Its experimental tractability, combined with the remarkable conservation of gene function throughout evolution, makes yeast the ideal model genetic organism. Yeast is a non-pathogenic model of fungal pathogens used to identify antifungal **targets** suitable for drug development and to elucidate mechanisms of action of antifungal agents. As a model of fundamental cellular processes and **metabolic pathways** of the human, yeast has improved our understanding and facilitated the molecular analysis of many disease genes. The completion of the Saccharomyces genome sequence helped launch the post-genomic era,

focusing on functional analyses of whole genomes. Yeast paved the way for the systematic analysis of large and complex genomes by serving as a test bed for novel experimental approaches and technologies, tools that are fast becoming the standard in drug discovery research

L155 ANSWER 11 OF 49 MEDLINE
ACCESSION NUMBER: 2001245313 MEDLINE
DOCUMENT NUMBER: 21101324 PubMed ID: 11171870
TITLE: Sick genes, sick individuals or sick populations with chronic disease? The emergence of diabetes and high blood pressure in African-origin populations.
AUTHOR: Cruickshank J K; Mbanya J C; Wilks R; Balkau B; McFarlane-Anderson N; Forrester T
CORPORATE SOURCE: Clinical Epidemiology Unit, University of Manchester Medical School, Manchester M13 9PT, UK.. clinep@man.ac.uk
SOURCE: INTERNATIONAL JOURNAL OF EPIDEMIOLOGY, (2001 Feb) 30 (1) 111-7.
Journal code: 7802871. ISSN: 0300-5771.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB AIM AND METHODS: To discuss evidence for and against genetic 'causes' of type 2 diabetes, illustrated by standardized study of glucose intolerance and high blood pressure in four representative African origin populations. Comparison of two genetically closer sites: rural (site 1) and urban Cameroon (2); then Jamaica (3) and Caribbean migrants to Britain (80% from Jamaica-4). BACKGROUND: Alternatives to the reductionist search for genetic 'causes' of chronic disease include Rose's concept that populations give rise to 'sick' individuals. Twin studies offer little support to genetic hypotheses because monozygotic twins share more than genes in utero and suffer from ascertainment bias. Non-genetic intergenerational mechanisms include amniotic fluid growth factors and maternal exposures. Type 2 diabetes and hypertension incidence accelerate in low-risk European populations from body mass > or =23 kg/m2, well within 'desirable' limits. Transition from subsistence agriculture in West Africa occurred this century and from western hemisphere slavery only six generations ago, with slow escape from intergenerational poverty since. RESULTS: 'Caseness' increased clearly within and between genetically similar populations: age-adjusted diabetes rates were 0.8, 2.4, 8.5 and 16.4% for sites 1-4, respectively; for 'hypertension', rates were 7, 16, 21 and 34%, with small shifts in risk factors. Body mass index rose similarly. CONCLUSION: Energy imbalance and intergenerational socioeconomic influences are much more likely causes of diabetes (and most chronic disease) than ethnic/genetic variation, which does occur, poorly related to phenotype. The newer method of **'proteomics'** holds promise for identifying environmental triggers influencing gene products. Even in lower prevalence 'westernized' societies, genetic screening per se for diabetes/chronic disease is likely to be imprecise and inefficient hence unreliable and expensive.

L155 ANSWER 12 OF 49 MEDLINE
ACCESSION NUMBER: 2001573773 MEDLINE
DOCUMENT NUMBER: 21537958 PubMed ID: 11680901
TITLE: Identification of incompletely processed potential carboxypeptidase E substrates from CpEfat/CpEfat mice.
AUTHOR: Bures E J; Courchesne P L; Douglass J; Chen K; Davis M T; Jones M D; McGinley M D; Robinson J H; Spahr C S; Sun J; Wahl R C; Patterson S D

CORPORATE SOURCE: Departments of Biochemistry and Genetics, Amgen, Thousand Oaks, CA, USA.
SOURCE: Proteomics, (2001 Jan) 1 (1) 79-92.
Journal code: 101092707. ISSN: 1615-9853.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011030
Last Updated on STN: 20020123
Entered Medline: 20011218

AB In an attempt to identify peptides that may be involved in the obese phenotype observed in CpEfat/CpEfat mice (deficient in Carboxypeptidase E, CpE) samples from fourteen neuroendocrine tissues in wild-type and CpEfat/CpEfat mice were obtained. Peptides were purified from these tissues and potential CpE substrate peptides were enriched using an anhydrotrypsin column that captures peptides with basic C-termini. Bound peptides were subjected to tryptic digestion and followed by liquid chromatography-mass spectrometry analysis. The relative levels of CpEfat/CpEfat versus wild-type peptides were determined by comparison of the ion intensities. Peptide ions elevated in the CpEfat/CpEfat samples were identified by targeted liquid chromatography-tandem mass spectrometry. From those ions, 27 peptides derived from known neuropeptides (including CpE substrates) were identified, together with another 25 peptides from proteins not known to be components of the neuropeptide processing pathway. The known CpE substrates identified included the recently discovered proSAAS, granin-like neuroendocrine peptide precursor that inhibits prohormone processing. The approach demonstrated the feasibility of using an affinity-based method for identifying differences in specific classes of peptides between normal and mutant mice.

L155 ANSWER 13 OF 49 MEDLINE
ACCESSION NUMBER: 2000470748 MEDLINE
DOCUMENT NUMBER: 20432565 PubMed ID: 10974127
TITLE: Search and discovery strategies for biotechnology: the paradigm shift.
AUTHOR: Bull A T; Ward A C; Goodfellow M
CORPORATE SOURCE: Research School of Biosciences, University of Kent, Canterbury, Kent CT2 7NJ, United Kingdom..
A.T.Bull@ukc.ac.uk
SOURCE: MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS, (2000 Sep) 64 (3) 573-606. Ref: 508
Journal code: 9706653. ISSN: 1092-2172.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001002

AB Profound changes are occurring in the strategies that biotechnology-based industries are deploying in the search for exploitable biology and to discover new products and develop new or improved processes. The advances that have been made in the past decade in areas such as combinatorial chemistry, combinatorial biosynthesis, **metabolic pathway** engineering, gene shuffling, and directed evolution of proteins have caused some companies to consider withdrawing from natural product screening. In this review we examine the paradigm shift from traditional

biology to bioinformatics that is revolutionizing exploitable biology. We conclude that the reinvigorated means of detecting novel organisms, novel chemical structures, and novel biocatalytic activities will ensure that natural products will continue to be a primary resource for biotechnology. The paradigm shift has been driven by a convergence of complementary technologies, exemplified by DNA sequencing and amplification, genome sequencing and annotation, **proteome** analysis, and phenotypic inventorying, resulting in the establishment of huge databases that can be mined in order to generate useful knowledge such as the identity and characterization of organisms and the identity of biotechnology **targets**. Concurrently there have been major advances in understanding the extent of microbial diversity, how uncultured organisms might be grown, and how expression of the metabolic potential of microorganisms can be maximized. The integration of information from complementary databases presents a significant challenge. Such integration should facilitate answers to complex questions involving sequence, biochemical, physiological, taxonomic, and ecological information of the sort posed in exploitable biology. The paradigm shift which we discuss is not absolute in the sense that it will replace established microbiology; rather, it reinforces our view that innovative microbiology is essential for releasing the potential of microbial diversity for biotechnology penetration throughout industry. Various of these issues are considered with reference to deep-sea microbiology and biotechnology.

L155 ANSWER 14 OF 49 MEDLINE
ACCESSION NUMBER: 2001227515 MEDLINE
DOCUMENT NUMBER: 21151076 PubMed ID: 11256578
TITLE: The use of **proteomics** in ophthalmic research.
AUTHOR: Steely H T Jr; Clark A F
CORPORATE SOURCE: Alcon Research Ltd, Fort Worth, TX 76134, USA..
tom.steely@alconlabs.com
SOURCE: Pharmacogenomics, (2000 Aug) 1 (3) 267-80. Ref: 61
Journal code: 100897350. ISSN: 1462-2416.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

AB The goal of molecular ophthalmology is the early detection and therapeutic treatment of eye disease. Genomic technologies have profoundly enhanced the discovery of ocular disease candidate genes. **Proteomics**, the protein cognate of genomic technology, offers a means to monitor changes in the expression of a given ocular protein(s) and its post-translational modification, identify novel therapeutic **targets** and evaluate pharmacological effects on a given **metabolic pathway**. Using both tissue and cultured cells, numerous laboratories have begun to catalogue changes in ocular protein expression in normal, diseased and ageing subjects. Herein, we review published **proteomic** literature in the broad context of ophthalmic diseases involving various tissues of the eye.

L155 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:964606 CAPLUS
DOCUMENT NUMBER: 138:35730
TITLE: Mitochondrial protein **targets** for drug screening and therapeutic intervention identified using mass spectrometry
INVENTOR(S): Gibson, Bradford W.; Ghosh, Soumitra S.; Davis, Robert

E.
PATENT ASSIGNEE(S): Mitokor, USA; The Regents of the University of California
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002101356	A2	20021219	WO 2002-US18484	20020610

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-296867P P 20010608

AB The invention concerns mitochondrial targets for drug screening assays and for therapeutic intervention in the treatment of diseases assocd. with altered mitochondrial function are provided by generating a high-resoln. (2-D) map of mitochondrial proteins, and then isolating at least one protein and subjecting it to mass spectrometric anal., including MALDI-TOF MS. Complete amino acid sequences [SEQ ID NOS:1-8] of polypeptides that comprise the human mitochondrial **proteome** are provided, using protein and peptide fractions of biol. samples derived from mitochondrial cybrid (cytoplasmic hybrid) cell lines, to identify previously unrecognized mitochondrial mol. components, including modified polypeptides that exhibit structural and/or functional alterations in diseases assocd. with altered mitochondrial function.

L155 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:814163 CAPLUS
DOCUMENT NUMBER: 137:322269
TITLE: Selective covalent-binding compounds having therapeutic, diagnostic and analytical applications
INVENTOR(S): Green, Bernard S.
PATENT ASSIGNEE(S): Semorex Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083708	A2	20021024	WO 2002-IL307	20020416

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-283645P P 20010416
AB Novel compds. are provided having enhanced affinity for a desired, preselected, target substance (a small mol.; a macromol. such as a protein, a carbohydrate, a nucleic acid, a cell, a viral particle, etc.) by modification with chem. groups that allow these substances to form strong bonds, such as irreversible covalent bonds, with the desired target substance. These qualities of tight, specific binding are reminiscent of antibody-like affinity; hence the new substances are termed COBALT, an acronym for covalent-binding antibody-like trap. The present invention includes a process wherein a target species is chosen and then, by synthetic chem. procedures and modifications, novel substances (COBALTs) are obtained that exhibit selective and covalent binding to the preselected target species. The applications of the COBALTs include diagnostic, anal., therapeutic and industrial applications. Cholesterol-binding molecularly-imprinted polymer MS50 was prepd. by polymn. of cholesteryl (4-vinyl)phenyl carbamate (template monomer), EGDM and cholesteryl methacrylate to make polymer MS41 and subsequent removal of the cholesterol from the carbamate in polymer MS41. COBALTs MS71 and MS80 were made by reaction of MS50 with triphosgene and thiophosgene, resp., for better cholesterol binding activity.

L155 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:754418 CAPLUS
DOCUMENT NUMBER: 137:289983
TITLE: Complete genome of Streptococcus pneumoniae and its proteins and nucleic acids and their uses for diagnosis infection and antibiotic targets
INVENTOR(S): Masignani, Vega; Tettelin, Herve; Fraser, Claire
PATENT ASSIGNEE(S): Chiron Spa, Italy; The Institute for Genomic Research
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077021	A2	20021003	WO 2002-IB2163	20020327

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-7658 A 20010327
AB The invention provides the sequences for 2489 proteins and their genes from Streptococcus pneumoniae type 4 strain JNR.7/87, together with the genome sequence comprising 2,162,598 bases in length. Gene knockout mutants indicate several essential genes which may be of value as preferred antibiotic targets. These proteins and genes are useful for the development of vaccines, diagnostics, and antibiotics.

L155 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:637801 CAPLUS
DOCUMENT NUMBER: 137:180780
TITLE: Collections of transgenic animal lines in which a subset of cells characterized by expression of an

endogenous "characterizing" gene and uses
INVENTOR(S): Serafini, Tito Andrew
PATENT ASSIGNEE(S): Renovis, Inc., USA
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064749	A2	20020822	WO 2002-US4765	20020214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-783487 A 20010214

AB The invention provides lines of transgenic animals, preferably mice, in which a subset of cells characterized by expression of a particular endogenous gene (a "characterizing gene") expresses, either constitutively or conditionally, a "system gene," which preferably encodes a detectable or selectable marker or a protein product that induces or suppresses the expression of a detectable or selectable marker (e.g., the protein product is a transcription factor and the expression of the detectable or selectable marker, or suppression thereof is dependent upon the transcription factor, for example, the nucleotide sequence encoding the detectable or selectable marker is operatively linked to a regulatory element recognized by the system gene product) allowing detection, isolation and/or selection of the subset of cells from the other cells of the transgenic animal, or explanted tissue thereof. In a preferred embodiment, the transgene introduced into the transgenic animal includes at least the coding region sequences for the system gene product operably linked to all or a portion of the regulatory sequences from the characterizing gene such that the system gene has the same pattern of expression within the animal (i.e., is expressed substantially in the same population of cells) or within the anatomical region contg. the cells to be analyzed as the characterizing gene. The invention provides collections of such lines of transgenic animals and vectors for producing them, and also provides methods for the detection, isolation and/or selection of a subset of cells expressing the marker gene in such transgenic animal lines. The vector (preferably a BAC) comprising the system gene coding sequences and characterizing gene sequences is then introduced into the genome of a potential founder animal to generate a line of transgenic animals. Also, preferably, the transgene contg. the system gene coding sequences and characterizing gene sequences is present in the genome at a site other than where the endogenous characterizing gene is located. Such transgenic animals can then be used to detect, isolate and/or select pure populations of cells having a particular functional characteristic, preferably cells of the nervous system. Creation of transgenic mouse line expressing a 5HT2A receptor BAC was demonstrated. The isolated cells have uses in gene discovery, target identification and validation, genomic and **proteomics** anal., etc.

L155 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:276137 CAPLUS

DOCUMENT NUMBER: 136:305090
TITLE: Whole cell engineering by mutagenizing a substantial portion of a starting genome and combining mutations with optional reiteration, identifying protein profiles by differential labeling and mass spectrometry, and by metabolic flux analysis
INVENTOR(S): Short, Jay M.; Fu, Pengcheng; Latterich, Martin; Wei, Jing; Levin, Michael
PATENT ASSIGNEE(S): Diversa Corporation, USA
SOURCE: PCT Int. Appl., 869 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029032	A2	20020411	WO 2001-US31004	20011001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2001096551	A2	20011220	WO 2001-US19367	20010614
WO 2001096551	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2002011402	A5	20020415	AU 2002-11402	20011001

PRIORITY APPLN. INFO.:
US 2000-677584 A2 20000930
US 2001-279702P P 20010328
WO 2001-US19367 W 20010614
US 2000-594459 A2 20000614
WO 2001-US31004 W 20011001

OTHER SOURCE(S): MARPAT 136:305090

AB An invention comprising cellular transformation, directed evolution, and screening methods for creating novel transgenic organisms having desirable properties. In one embodiment, this invention provides a method of generating a transgenic organism, such as a microbe or a plant, having a plurality of traits that are differentially activatable. This invention also provides a method of retooling genes and gene pathways by the introduction of regulatory sequences, such as promoters, that are operable in an intended host, this conferring operability to a novel gene pathway when it is introduced into an intended host. For example a novel man-made gene pathway, generated based on microbially-derived progenitor templates, that is operable in a plant cell. This invention also provides a method of generating novel host organisms having increased expression of desirable traits, recombinant genes, and gene products. This invention provides novel methods for detg. polypeptide profiles, and protein expression variations, which methods are applicable to all sample types disclosed herein. The present invention provides methods of simultaneously identifying and quantifying individual proteins in complex protein mixts. by fragmentation, differential labeling, and tandem mass

spectrometry. Addnl. this invention provides methods for cellular and metabolic engineering of new and modified phenotypes by using "online" or "real-time" metabolic flux anal.

L155 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:833395 CAPLUS
DOCUMENT NUMBER: 137:348834
TITLE: Process for diagnosis of physiological conditions by characterization of **proteomic** materials
INVENTOR(S): Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002160420	A1	20021031	US 2001-846330	20010430
WO 2002088744	A2	20021107	WO 2002-CA623	20020429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846330 A 20010430
AB The present invention discloses the use of **proteomic** investigation as a diagnostic tool; and particularly teaches the use of **proteomic** investigative techniques and methodol. to det. a **proteomic** basis for the development and progression of abnormal physiol. conditions and the development and characterization of risk assessment, diagnostic and therapeutic means and methodologies. Serum samples from patients suffering from a variety of diseases in Syndrome X were analyzed by SELDI mass spectrometry using the Ciphergen PROTEINCHIP system to discern disease markers.

L155 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:488167 CAPLUS
DOCUMENT NUMBER: 137:57524
TITLE: Drug evaluation operating principles
INVENTOR(S): Ernest, Michael; Slate, Doris L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002081750	A1	20020627	US 2001-956094	20010920

PRIORITY APPLN. INFO.: US 2000-257166P P 20001222
AB The present invention relates to methods for detg. whether a drug candidate should be advanced from discovery through evaluation to development and marketing. In one embodiment of the present invention,

the drug development methods utilize a team decision-making format wherein scientific staff, and regulatory, financial, and marketing personnel may contribute to the evaluation of a new drug compd. In another embodiment of the methods of the present invention, decisions concerning the future of a potential drug may be made at earlier designated timepoints in the evaluation process, and these decisions may be made based on criteria such as preclin. pharmacol. and toxicol. data. In a further embodiment of the present invention, the potential new drug may be assigned a risk characterization, such as a color code, which defines the extent and duration of the evaluation process.

L155 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:294164 CAPLUS
DOCUMENT NUMBER: 136:304030
TITLE: Methods for validating polypeptide **targets** that correlate to cellular phenotypes utilizing yeast two-hybrid protein interaction assays, and uses thereof in high-throughput drug screening
INVENTOR(S): Kamb, Carl Alexander; Caponigro, Giordano Michael; Teng, David Heng-fai; Sandrock, Tanya Marie; Stump, Mark
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 193,759, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045188	A1	20020418	US 2001-865644	20010525
WO 2000029565	A1	20000525	WO 1999-US27409	19991117

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-193759 B2 19981117
WO 1999-US27409 W 19991117

AB The invention provides methods for screening for physiol. relevant intermol. interactions with phenotype probes and yeast two-hybrid protein interaction assays. These interactions often are between an endogenous protein or other proteinaceous mol. (referred to herein as an "endogenous protein") and one or more corresponding ligands. Such endogenous protein-ligand interactions often participate in or indirectly affect an endogenous cellular pathway of interest. Such physiol. relevant protein-ligand interactions are detected and validated by using two independent phenotypic probes to identify and eliminate non-relevant interactions, or by interaction with a single probe when the identity of the endogenous protein as a candidate target was previously known. The invention also provides method for constructing four yeast two-hybrid reporter plasmids that are designed for use in a Gal4-based reporter system or a LexA-based reporter system. The methods are particularly valuable for assays involving endogenous mammalian proteins, and for streamlining and focusing high-throughput screening procedures.

L155 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:948944 CAPLUS
DOCUMENT NUMBER: 138:50913
TITLE: Sequence of the genome of Streptococcus agalactiae and application to the development of vaccines and diagnostic tools and for identification of therapeutic targets
INVENTOR(S): Glaser, Philippe; Rusniok, Christophe; Chevalier, Fabien; Frangeul, Lionel; Lalioui, Lila; Zouine, Mohammed; Couve, Elisabeth; Buchrieser, Carmen; Poyart, Claire; Trieu, Cuot Patrick
PATENT ASSIGNEE(S): Institut Pasteur, Fr.
SOURCE: Fr. Demande, 2687 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2824074	A1	20021031	FR 2001-5642	20010426
WO 2002092818	A2	20021121	WO 2002-IB3059	20020426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2001-5642 A 20010426
AB The nearly complete sequence of the genome of Streptococcus agalactiae strain CIP 8245 (ATCC 12403) was detd. by shotgun sequencing. The 2.2-Mb chromosome is represented by 138 contigs, and a plasmid genome comprising 45 kbp by a single contig. Addnl., the sequences of 2205 proteins encoded by open reading frames within the genome are provided. Characterization of the genome and its encoded proteome provide the basis for detection and/or amplification of Streptococcus bacteria, and in particular S. agalactiae, cloning and expression vectors for genetic transformation, antibodies for use in immunoassays of Streptococcus bacteria, and development of pharmaceuticals and/or vaccines for inhibition of S. agalactiae infection of animals or humans.

L155 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:351750 CAPLUS
DOCUMENT NUMBER: 132:345171
TITLE: Separation, screening, and identification of biological targets
INVENTOR(S): Champagne, James T.
PATENT ASSIGNEE(S): Proteo Tools, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029848	A1	20000525	WO 1999-US27192	19991117

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-108889P P 19981117

AB The present invention relates to the field of **proteomics**. More specifically, the present invention describes methods and app. for the isolation, characterizing, screening, recombining and interacting of biol. mols. such as proteins, peptides, nucleic acids and ligands so as to analyze various biol. activities of these mols. individually or on a cellular scale. Moreover, the invention relates to the positional mapping of isolated biol. mols. in multiple soln.-base sepn. means so as to provide a unique set of identifying characteristics for each biol. mol. in a system. The invention further relates to the utilization of this information for the simultaneous screening, selection and enrichment of interactive ligands, substrates or other interactive mols. in many thousands of parallel ligand-target, substrate-enzyme or other biol. interactions. The invention further relates to identification and display of the target mols. or interactive mols. for subsequent anal. The present invention is valuable in the screening and study of potential small therapeutic mols. and their interactions in various cell types of choice.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L155 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:405112 CAPLUS
DOCUMENT NUMBER: 131:56155
TITLE: Methods for the simultaneous identification of novel biological **targets** and lead structures for drug development using combinatorial libraries and probes
INVENTOR(S): Heefner, Donald L.; Zepp, Charles M.; Gao, Yun; Jones, Steven W.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931267	A1	19990624	WO 1998-US26894	19981218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2314422	AA	19990624	CA 1998-2314422	19981218
AU 9919256	A1	19990705	AU 1999-19256	19981218
EP 1049796	A1	20001108	EP 1998-964053	19981218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508507	T2	20020319	JP 2000-539165	19981218

PRIORITY APPLN. INFO.: US 1997-68035P P 19971218
WO 1998-US26894 W 19981218

AB The combinatorial screening assays and detection methods of the present

invention encompass highly diversified libraries of compds. which act as fingerprints to allow for the identification of specific mol. differences existing between biol. samples. The combinatorial screening assay and detection methods of the present invention utilize highly diversified libraries of compds. to interrogate and characterize complex mixts. in order to identify specific mol. differences existing between biol. samples, which may serve as targets for diagnosis of development of therapeutics. The invention is base, in part, on the design of sensitive, rapid, homogeneous assay systems that permit the evaluation, interrogation, and characterization of samples using complex, highly diversified libraries of mol. probes. The ability to run the high throughput assays in a homogeneous format increases sensitivity of screening. In addn., the homogeneous format allows the mols. which interact to maintain their native or active conformations. Moreover, the homogeneous assay systems of the invention utilize robust detection systems that do not require sepn. steps for detection of reaction products. The assays of the invention can be used for diagnostics, drug screening and discovery, target-driven discover, and in the field of **proteomics** and genomics for the identification of disease markers and drug targets.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L155 ANSWER 26 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002347686 EMBASE
TITLE: New routes for drug discovery.
AUTHOR: Jain K.K.
CORPORATE SOURCE: K.K. Jain, Blasiring 7, CH-4057 Basel, Switzerland. jain@pharmabiotech.ch
SOURCE: Drug Discovery Today, (1 Sep 2002) 7/17 (900-902). Refs: 4
ISSN: 1359-6446 CODEN: DDTOFS
PUBLISHER IDENT.: S 1359-6446(02)02354-1
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

L155 ANSWER 27 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002400688 EMBASE
TITLE: NIDDK encourages technology research in diabetes.
AUTHOR: Fradkin J.
CORPORATE SOURCE: Dr. J. Fradkin, Division of Diabetes, NIDDK, MSC 2560, 31 Center Drive, Bethesda, MD 20892, United States. JF58S@nih.gov
SOURCE: Diabetes Technology and Therapeutics, (2002) 4/5 (713-716). ISSN: 1520-9156 CODEN: DTTHFH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) actively supports technology-related research directed at development of new therapies for prevention and treatment of diabetes and its complications. Identification of the genetic and environmental contributors to diabetes and the molecular mechanisms through which they act will yield new targets for therapeutic development. Major efforts are also directed at development of .beta.-cell replacement therapy; improved methods for sensing glucose and delivering insulin; imaging technologies

and other surrogate markers to detect disease progression; improved animal models for study of diabetes and its complications; and clinical trials to evaluate the safety and efficacy of new therapies. Application of genomic, **proteomic** and other new technologies to diabetes research, collaborations between diabetes researchers and researchers with technologies relevant to diabetes, and bench to bedside translational research are particularly encouraged. A variety of funding mechanisms are available to prospective researchers.

L155 ANSWER 28 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002113345 EMBASE
TITLE: Toxicoproteomics - A new preclinical tool.
AUTHOR: Bandara L.R.; Kennedy S.
CORPORATE SOURCE: L.R. Bandara, Oxford GlycoSciences (UK), 86 Milton Park, Abingdon OX14 4RY, United Kingdom. lan.bandara@ogs.co.uk
SOURCE: Drug Discovery Today, (1 Apr 2002) 7/7 (411-418).
Refs: 54
ISSN: 1359-6446 CODEN: DDTOFS
PUBLISHER IDENT.: S 1359-6446(02)02211-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The publication of the human genome has presented the scientific community with an unprecedented amount of genetic information with the potential to revolutionize the drug discovery process. This information could be used to identify novel drug targets and disease markers or could aid in the development of personalized medicines. The realization that genetic changes must ultimately influence protein function has pushed the field of **proteomics** further into the limelight. In this review the applications of **proteomics** to the field of toxicology will be discussed. It is anticipated that, in the future, toxicologists will apply a range of genomic and **proteomic** techniques to address issues in toxicity.

L155 ANSWER 29 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002400297 EMBASE
TITLE: **Proteomic** approaches to central nervous system disorders.
AUTHOR: Rohlff C.; Southan C.
CORPORATE SOURCE: C. Rohlff, Oxford GlycoSciences, 86 Milton Park, Abingdon OX14 4RY, United Kingdom. Christian.Rohlff@ogs.co.uk
SOURCE: Current Opinion in Molecular Therapeutics, (2002) 4/3 (251-258).
Refs: 33
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The discovery, design and evaluation of new medicines is critically dependent on the elucidation of protein mechanisms involved in human diseases. Since the **proteome** of a cell or tissue is not a simple reflection of its transcriptome, direct protein-based analysis is needed. Advances in **proteomic** technologies are improving the analysis of membrane proteins and signaling complexes with increased speed and molecular detail. Changes in protein isoforms due to post-translational modifications, such as phosphorylation induced by cell signaling events

and alternative spliceforms of receptors, may be mapped to an altered protein expression pattern in clinically relevant cell populations with a causative or diagnostic disease link. A CNS **proteome** database derived from primary human tissues may avoid ambiguities of experimental models. It will also accelerate the development of more specific diagnostic and prognostic disease markers as well as new selective therapeutics. **Proteomics** is also being applied to resolve in silico gene prediction uncertainties by direct open reading frame verfication. These advances hold great promise for improvements in the understanding, diagnosis and therapy of central nervous system disorders.

L155 ANSWER 30 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002092943 EMBASE
TITLE: Metabolic control analysis in drug discovery and disease.
AUTHOR: Cascante M.; Boros L.G.; Comin-Anduix B.; De Atauri P.; Centelles J.J.; Lee P.W.-N.
CORPORATE SOURCE: M. Cascante, Department of Biochemistry, CeRQT - Parc de Barcelona (PCB), University of Barcelona, Marti i Franques 1, Barcelona, Catalonia 08028, Spain
SOURCE: Nature Biotechnology, (2002) 20/3 (243-249).
Refs: 70
ISSN: 1087-0156 CODEN: NABIF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Metabolic control analysis (MCA) provides a quantitative description of substrate flux in response to changes in system parameters of complex enzyme systems. Medical applications of the approach include the following: understanding the threshold effect in the manifestation of metabolic diseases; investigating the gene dose effect of aneuploidy in inducing phenotypic transformation in cancer; correlating the contributions of individual genes and phenotypic characteristics in metabolic disease (e.g., diabetes); identifying candidate enzymes in pathways suitable as targets for cancer therapy; and elucidating the function of "silent" genes by identifying metabolic features shared with genes of known pathways. MCA complements current studies of genomics and **proteomics**, providing a link between biochemistry and functional genomics that relates the expression of genes and gene products to cellular biochemical and physiological events. Thus, it is an important tool for the study of genotype-phenotype correlations. It allows genes to be ranked according to their importance in controlling and regulating cellular metabolic networks. We can expect that MCA will have an increasing impact on the choice of targets for intervention in drug discovery.

L155 ANSWER 31 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002400290 EMBASE
TITLE: Recent advances in oncoproteomics.
AUTHOR: Jain K.K.
CORPORATE SOURCE: K.K. Jain, PharmaBiotech, Blasiring 7, CH-4057 Basel, Switzerland. jain@pharmabiotech.ch
SOURCE: Current Opinion in Molecular Therapeutics, (2002) 4/3 (203-209).
Refs: 31
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer

022 Human Genetics
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Advances in **proteomics** are contributing to the understanding of pathophysiology of cancer, cancer diagnosis and anticancer drug discovery. Laser capture microdissection (LCM) provides an ideal method for extraction of cells from specimens in which the exact morphologies of both the captured cells and the surrounding tissue are preserved. Differentially expressed proteins in tumor tissue are found by comparing the protein expression patterns generated using SELDI (surface-enhanced laser desorption/ionization)-based protein chip technology. **Proteomic** technologies have been used for the study of cancer of various organs. Continued refinement of techniques and methods to determine the abundance and status of proteins in vivo holds great promise for future study of cancer and development of personalized cancer therapies.

L155 ANSWER 32 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002185785 EMBASE
TITLE: LabAutomation 2002. Productive technologies for the New Millenium.
AUTHOR: Kempner M.E.; Felder R.A.
SOURCE: JALA - Journal of the Association for Laboratory Automation, (2002) 7/2 (38-49).
ISSN: 1535-5535 CODEN: JALLFO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
022 Human Genetics
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: English

L155 ANSWER 33 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001282203 EMBASE
TITLE: **Proteomics**: Delivering new routes to drug discovery - Part 2.
AUTHOR: Jain K.K.
CORPORATE SOURCE: K.K. Jain, Blasiring 7, CH-4057 Basel, Switzerland. jain@pharmabiotech.ch
SOURCE: Drug Discovery Today, (15 Aug 2001) 6/16 (829-832).
Refs: 11
ISSN: 1359-6446 CODEN: DDTOFS
PUBLISHER IDENT.: S 1359-6446(01)01912-2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
029 Clinical Biochemistry
003 Endocrinology
LANGUAGE: English

L155 ANSWER 34 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002017836 EMBASE
TITLE: Editorial overview: Genomics and **proteomics**.
AUTHOR: Cowsert L.; Huber L.
CORPORATE SOURCE: L. Cowsert, VistaGen Inc., 1450 Rollins Road, Burlingame, CA 94010-2307, United States. lcowsert@vistagen-inc.com

SOURCE: Current Opinion in Molecular Therapeutics, (2001) 3/6 (524-525).
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L155 ANSWER 35 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002004392 EMBASE
TITLE: Pseudomonas aeruginosa and a **proteomic** approach to bacterial pathogenesis.
AUTHOR: Sherman N.E.; Stefansson B.; Fox J.W.; Goldberg J.B.
CORPORATE SOURCE: J.B. Goldberg, Department of Microbiology, University of Virginia Health System, Charlottesville, VA 22908, United States. jbg2b@virginia.edu
SOURCE: Disease Markers, (2001) 17/4 (285-293).
Refs: 29
ISSN: 0278-0240 CODEN: DMARD3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Pseudomonas aeruginosa is a Gram-negative bacterium that is ubiquitous in the environment and can cause a variety of diseases in compromised patients. The genome of P. aeruginosa strain PAO1 has been reported to contain 5570 potential proteins. The value of this genomic database is that new proteins can be recognized to use as diagnostic markers, novel drug targets, and to better understand the physiology of this organism. However, similar to what has been observed in other sequenced bacterial genomes, approximately one third of the potential proteins have no known function. This is somewhat surprising given the long-standing interest in P. aeruginosa as an opportunistic pathogen. Obviously new tools, in addition to sequence similarity analysis, are needed to determine the role of these proteins. **Proteomics** using two-dimensional gel electrophoresis followed by mass spectrometry to detect and identify P. aeruginosa proteins represents a novel approach to address this gap.

L155 ANSWER 36 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001253078 EMBASE
TITLE: Drug discovery and target validation.
AUTHOR: Nuttall M.E.
CORPORATE SOURCE: Dr. M.E. Nuttall, GlaxoSmithKline Pharmaceuticals, 709 Swedeland Road, King of Prussia, PA 19406, United States. mark_e_nuttall@sbphrd.com
SOURCE: Cells Tissues Organs, (2001) 169/3 (265-271).
Refs: 15
ISSN: 1422-6405 CODEN: CTORFB
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 031 Arthritis and Rheumatism
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recent drug discovery has been driven largely by a genomics-based approach. This revolution in pharmaceutics is based on localized expression of either a novel gene or homologue of a known gene found in cDNA libraries made from normal versus diseased tissue. The choice and

quality of cDNA library is critical for the success of this approach. Expression is normally verified at the cellular level by either immunocytochemistry or in situ hybridization. Activity of the recombinant protein in secondary cell-based assays allows highthroughput screens to be formulated to identify small-molecule effectors of this protein. More recently, a **proteomics** approach has also been incorporated into this process. This technology directly measures proteins whose expression is localized in disease tissue as the basis for cell-based screens to look for either activators or inhibitors, of this activity. The majority of screens are designed to look for inhibitors. Activity of small-molecules found by screening gives rise to pharmacokinetic studies and verification of activity in animal models of the disease. Structure-activity relationship (SAR) optimization of these small-molecules allows for suitable oral bioavailability and pharmacokinetics, resulting in compounds progressing from discovery to development. Based on these strategies, we have developed inhibitors of osteoclast-mediated bone resorption and are currently screening for bone anabolic agents. In addition, we have also developed small-molecule caspase inhibitors which prevent chondrocyte apoptosis and retain cell function in an attempt to find therapeutic agents to either prevent or treat osteoarthritis. These agents may well have utility in the treatment of temporomandibular joint diseases.

L155 ANSWER 37 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001167154 EMBASE
TITLE: Preface.
AUTHOR: Roth B.D.; Sliskovic D.R.
CORPORATE SOURCE: B.D. Roth, Pfizer, Global Research and Development, Ann Arbor Laboratories, Ann Arbor, MI, United States
SOURCE: Current Pharmaceutical Design, (2001) 7/4 (xxx).
ISSN: 1381-6128 CODEN: CPDEFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 003 Endocrinology
016 Cancer
028 Urology and Nephrology
029 Clinical Biochemistry
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

L155 ANSWER 38 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000424627 EMBASE
TITLE: **Proteomics**: A new approach to the study of disease.
AUTHOR: Chambers G.; Lawrie L.; Cash P.; Murray G.I.
CORPORATE SOURCE: Dr. G.I. Murray, Department of Pathology, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, United Kingdom. g.i.murray@abdn.ac.uk
SOURCE: Journal of Pathology, (2000) 192/3 (280-288).
Refs: 67
ISSN: 0022-3417 CODEN: JPTLAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The global analysis of cellular proteins has recently been termed **proteomics** and is a key area of research that is developing in the post-genome era. **Proteomics** uses a combination of sophisticated techniques including two-dimensional (2D) gel electrophoresis, image

analysis, mass spectrometry, amino acid sequencing, and bio-informatics to resolve comprehensively, to quantify, and to characterize proteins. The application of **proteomics** provides major opportunities to elucidate disease mechanisms and to identify new diagnostic markers and therapeutic targets. This review aims to explain briefly the background to **proteomics** and then to outline **proteomic** techniques. Applications to the study of human disease conditions ranging from cancer to infectious diseases are reviewed. Finally, possible future advances are briefly considered, especially those which may lead to faster sample throughput and increased sensitivity for the detection of individual proteins. Copyright (C) 2000 John Wiley and Sons, Ltd.

L155 ANSWER 39 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999190307 EMBASE
TITLE: Division of medicinal chemistry - Functional Genomics/ **Proteomics.**
AUTHOR: Fernandes P.B.
CORPORATE SOURCE: P.B. Fernandes, Small Molecule Therapeutics Inc, 11 Deer Park Drive, Monmouth Junction, NJ 08852, United States. fernandes@smtherapeutics.com
SOURCE: IDrugs, (1999) 2/6 (511-514).
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The presentations and discussion satisfied the objectives of the symposium. Scientists now have several ways to identify new drug discovery targets from gene sequences. The entry of chemists into the functional genomics and **proteomics** area will be central to the development of drugs targeted to the new sites emerging from studies on the human genome.

L155 ANSWER 40 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999288504 EMBASE
TITLE: Future prospects for the chemotherapy of Chagas' disease.
AUTHOR: Fairlamb A.H.
CORPORATE SOURCE: Dr. A.H. Fairlamb, Department of Biochemistry, Wellcome Trust Building, University of Fundee, Dundee DD1 5EH, United Kingdom
SOURCE: Medicina, (1999) 59/SUPPL. 2 (179-187).
Refs: 108
ISSN: 0025-7680 CODEN: MEDCAD
COUNTRY: Argentina
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Spanish
AB Over the last two decades, progress towards new drugs for the treatment of Chagas' disease has been disappointing. However, as a result of the parasite genome sequencing projects, the possibility of identifying novel drug targets through genomics, **proteomics** and bioinformatics has never been better. Progress towards the development of novel therapeutics, from target identification and validation by chemical and genetic means through to rational drug design, is illustrated with reference to the metabolism and functions of trypanothione, with particular emphasis on trypanothione reductase, one current drug target of choice.

L155 ANSWER 41 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-723209 [78] WPIDS
CROSS REFERENCE: 2002-691674 [74]
DOC. NO. NON-CPI: N2002-570271
DOC. NO. CPI: C2002-204702
TITLE: Pumping device, e.g. for analyzing biological sample, comprises substrate having walls which define microchannel and two electrodes positioned to form first capacitor having electric field that traverses microchannel.
DERWENT CLASS: B04 D16 J04 P81 Q56 Q68
INVENTOR(S): KENNEY, J T; SAVILLE, D A; VACCA, G
PATENT ASSIGNEE(S): (LIGH-N) LIGHTWAVE MICROSYSTEMS CORP
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002068821	A2	20020906	(200278)*	EN	57

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002068821	A2	WO 2002-US7923	20020228

PRIORITY APPLN. INFO: US 2002-272337 20020227; US 2001-272337P 20010228

AB WO 200268821 A UPAB: 20021204
NOVELTY - Pumping device (I) comprising substrate with walls defining a microchannel and two electrodes positioned to form a first capacitor with an electric field traversing the microchannel that contains first and second fluids between the electrodes where the fluids have an interface between them and different dielectric constants so the interface moves in the presence of the electric field, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for moving a first fluid in a microchannel (100), by placing an interface formed by the first fluid and a second fluid in an electric field generated by a capacitor having a first plate at a first potential and a second plate at a second potential. The first and second fluids have dissimilar dielectric constants, such that the interface moves in the presence of the electric field.

USE - (I) is useful for moving a fluid volume within a microchannel in an optical telecommunications device or for moving a fluid volume within a microchannel to react or analyze a biological or chemical sample (claimed). It can be used in medical diagnostics, in which a volume of sample from a patient (e.g. droplet of blood) is processed within a microfluidic device. It can also be used in sampling air to determine the presence of pathogens or poisons by drawing in a sample of air and processing this fluid sample to identify whether DNA or another signature of interest (e.g. proteins uniquely associated with the pathogen) is present. It can be used in the fields of biological research, medical research, emerging fields of **proteomics** an high-throughput screening of e.g., **drugs** or chemicals to determine the interaction of these compounds with proteins and other compounds of interest (e.g. antibodies or chemicals involved in **metabolic**

pathways), and in the field of optical telecommunications and optical data transmission in which optical signals are used to convey information at the speed of light.

ADVANTAGE - (I) minimizes problems associated with contact-angle hysteresis. The movement of the fluids provides low power dissipation and the required material versatility.

DESCRIPTION OF DRAWING(S) - The figure illustrates a fluid-fluid interface in a microchannel.

Microchannel 100

Dwg.1/20

L155 ANSWER 42 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-463471 [49] WPIDS
DOC. NO. CPI: C2002-131831
TITLE: New human proteases useful for diagnosing, preventing or treating anorexia, myocardial infarction, Addison's disease, hepatitis, Cushing's syndrome, eczema, Parkinson's disease, and impotence.
DERWENT CLASS: B04 D16
INVENTOR(S): ARVIZU, C; AU-YOUNG, J; AZIMZAI, Y; BAUGHN, M R; BOROWSKY, M L; BURFORD, N; DELEGEANE, A M; ELILIOTT, V S; GANDHI, A R; GRIFFIN, J A; HAFALIA, A J A; ISON, C H; KALLICK, D A; KEARNEY, L; LAL, P G; LEE, E A; LEE, S; LO, T P; LU, D A M; LU, Y; NGUYEN, D B; RAMKUMAR, J; SWARNAKAR, A; TANG, Y T; THANGAVELU, K; TRIBOULEY, C M; WALIA, N K; WARREN, B A; XU, Y; YAO, M G; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002038744	A2	20020516	(200249)*	EN	168
AU 2002039753	A	20020521	(200260)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002038744	A2	WO 2001-US51034	20011018
AU 2002039753	A	AU 2002-39753	20011018

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002039753	A Based on	WO 200238744

PRIORITY APPLN. INFO: US 2000-250981P 20001201; US 2000-241573P 20001018; US 2000-243643P 20001025; US 2000-245256P 20001102; US 2000-248395P 20001113; US 2000-249826P 20001116; US 2000-252303P 20001120

AB WO 200238744 A UPAB: 20020802

NOVELTY - An isolated human proteases (PRTS) polypeptide (I), comprising a sequence (S1) of 334, 511, 812, 1236, 304, 980, 1251, 1128, 462, 659, 626, 557, 494, 593 or 319 amino acids, given in the specification, a naturally

occurring polypeptide comprising an amino acid sequence 90 % identical to (S1), or a biologically active or immunogenic fragment of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I) and comprising a sequence (S2) of 2406, 1967, 3446, 4888, 1074, 3573, 4659, 3711, 2017, 2646, 2088, 1890, 2984, 2255 or 1250 nucleotides, given in the specification, a naturally occurring polynucleotide comprising a polynucleotide sequence 90 % identical to (S2), a polynucleotide complementary to (II), or an RNA equivalent of (II);

(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) a cell transformed with (III);

(4) a transgenic organism comprising (III);

(5) producing (I);

(6) an isolated antibody (IV) which specifically binds to (I);

(7) an isolated polynucleotide (V) comprising 60 contiguous nucleotides of (II);

(8) detecting (M1) a target polynucleotide having the sequence of (II) in a sample, by:

(a) hybridizing the sample with a probe comprising 20 contiguous nucleotides comprising a sequence complementary to the target polynucleotide in the sample, where the probe specifically hybridizes to the target polynucleotide under conditions where a hybridization complex is formed between the probe and the target polynucleotide or its fragments, or by amplifying the target polynucleotide or its fragment by a polymerase chain reaction (PCR); and

(b) detecting the presence or absence of the hybridization complex or the amplified product, and, optionally, if present the amount of the complex or the amplified product;

(9) an antibody (VI) (monoclonal, polyclonal) produced by using (I);

(10) a composition (VII) comprising (I), (IV), (VI), an agonist or an antagonist compound (identified using (I));

(11) a microarray (VIII) in which an element of the microarray is (V); and

(12) an array (IX) comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, where one of the nucleotide molecules comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with 30 contiguous nucleotides of a target polynucleotide, and where the target polynucleotide is (II).

ACTIVITY - Antiinflammatory; Antiulcer; Antiarteriosclerotic; Hypotensive; Cardiant; Antianginal; Anti-HIV; Antiallergic; Antianemic; Antiasthmatic; Antithyroid; Virucide; Hepatotropic; Antipsoriatic; Cytostatic; Ophthalmological; Dermatological; Vulnerary; Cerebroprotective; Anticonvulsant; Antiparkinsonian; Nootropic; Neuroprotective; Antiinfertility; Vasotropic; Gynecological.

MECHANISM OF ACTION - Gene therapy; Protease modulator. No biological data is given.

USE - (I) is useful for screening a compound for effectiveness as an agonist or antagonist of (I), by exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample. (I), the identified agonist and antagonist are useful for treating a disease or condition associated with decreased or overexpression of functional PRTS in a patient. (I) is useful for screening for a compound that modulates the activity of the polypeptide or that binds to the polypeptide. (I) is also useful as an immunogen for preparing polyclonal or monoclonal antibodies by hybridoma technology. Nucleic acid (II) encoding (I) is useful for screening a compound for effectiveness in altering expression of a target polynucleotide comprising the sequence of (II). A probe comprising 20 contiguous nucleotides of (II) is useful for assessing toxicity of a test compound, by treating a biological sample containing nucleic acids with the test compound, hybridizing the probe with nucleic acids of the treated biological sample to form a complex, quantifying the

amount of hybridization complex and comparing the complex in the treated biological sample with the amount of complex in an untreated biological sample, where a difference in the amount of complex in the treated biological sample is indicative of toxicity of the test compound. An antibody (IV) that binds (I) is useful for detecting the presence of (I) and purifying (I) from a sample. (IV), optionally labeled is useful for diagnosing a condition or disease associated with expression of PRTS in a subject or in a biological sample. A microarray (VIII) is useful for generating an expression profile of a sample which contains polynucleotides (all claimed). (I) and (II) and modulators of (I) are useful for diagnosis, treatment and prevention of:

(i) gastrointestinal disorder such as dysphagia, gastritis, anorexia, pancreatitis, ulcerative colitis, Reye's syndrome, etc;

(ii) cardiovascular such as atherosclerosis, **hypertension**, congestive heart failure, myocardial infarction, cardiomyopathy, angina pectoris, etc;

(iii) autoimmune/inflammatory disorders such as acquired immunodeficiency syndrome (AIDS), Addison's disease, allergies, anemia, asthma, bronchitis, Grave's disease, etc;

(iv) cell proliferative disorders such as arteriosclerosis, hepatitis, cirrhosis, myeloma, psoriasis, leukemia, etc;

(v) developmental disorder such as renal tubular acidosis, Cushing's syndrome, gonadal dysgenesis, cataract, etc;

(vi) epithelial disorders such as allergic contact dermatitis, keloid, scabies, squamous cell carcinoma, eczema, etc;

(vii) neurological disorders such as stroke, epilepsy, Parkinson's disease, dementia, Alzheimer's disease, Huntington's disease, multiple sclerosis, etc; or

(viii) reproductive disorder such as infertility, disruption of the estrous cycle, ectopic pregnancy, prostatitis, gynecomastia, impotence, disruption of menstrual cycle, etc.

(I) is useful to analyze a **proteome** of a tissue or cell type. (II) is useful for creating knockin humanized animals or transgenic animals to model human disease and to detect and quantify gene expression in biopsied tissues in which expression of PRTS is correlated with disease. (II) is also useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence and oligonucleotide primers derived from (II) are useful to detect single nucleotide polymorphisms. PRTS, fragments of it and antibodies specific for PRTS are useful as elements on a microarray which is useful to monitor or measure **protein-protein** interactions, **drug-target** interactions and gene expression profiles. (II) is useful to generate a transcript image of a tissue or cell type.

Dwg.0/0

L155 ANSWER 43 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-097640 [13] WPIDS
DOC. NO. CPI: C2002-030429
TITLE: Novel human neurotransmitter transporter polypeptides and polynucleotides for diagnosing, preventing or treating transport, neurological and psychiatric disorders and for identifying modulators of therapeutic use.
DERWENT CLASS: B04 D16
INVENTOR(S): BAUGHN, M R; DING, L; ELLIOTT, V S; GANDHI, A R; HAFALIA, A; LAL, P; PATTERSON, C; RANKUMAR, J; SANJANWALA, M S; TRIBOULEY, C M; WALIA, N K; YAO, M G; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001090148	A2	20011129	(200213)*	EN	123

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001063310 A 20011203 (200221)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001090148	A2	WO 2001-US16283	20010517
AU 2001063310	A	AU 2001-63310	20010517

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001063310	A	Based on	WO 200190148

PRIORITY APPLN. INFO: US 2000-221488P 20000727; US 2000-205518P 20000519; US 2000-213956P 20000622; US 2000-215105P 20000628; US 2000-218947P 20000714; US 2000-220448P 20000727

AB WO 200190148 A UPAB: 20020711
NOVELTY - An isolated human neurotransmitter transporter polypeptide (I), (NTT) 1-6, comprising a sequence (S1) of 602, 730, 523, 649, 625 or 592 amino acids defined in the specification, a naturally occurring polypeptide comprising an amino acid sequence 90% identical to (S1), a biologically active or immunogenic fragment of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I) and comprising a sequence (S2) of 2168, 2709, 2958, 2135, 1997 or 2774 base pairs (bp) defined in the specification, a naturally occurring polynucleotide comprising a polynucleotide sequence 90% identical to (S2), a polynucleotide complementary to (II) or an RNA equivalent of (II);

(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) a cell transformed with (III);

(4) a transgenic organism comprising (III);

(5) method of producing (I);

(6) an isolated antibody (IV) which specifically binds to (I);

(7) an isolated polynucleotide comprising at least 60 contiguous nucleotides of (II);

(8) detecting (M1) a target polynucleotide having the sequence of (II) in a sample, by:

(a) hybridizing the sample with a probe comprising 20 contiguous nucleotides comprising a sequence complementary to the target polynucleotide in the sample, where the probe specifically hybridizes to the target polynucleotide under conditions where a hybridization complex is formed between the probe and the target polynucleotide or its fragments, or by amplifying the target polynucleotide or its fragment by PCR; and

(b) detecting the presence or absence of the hybridization complex or the amplified product, and, optionally, if present the amount of the complex or the amplified product;

(9) an antibody (monoclonal) produced by using (I); and

(10) a composition comprising (I), an agonist or antagonist compound identified using (I), (IV) or the above antibody.

ACTIVITY - **Antidiabetic**; Antiparkinsonian; Antianginal; Neuroprotective; Nootropic; Antidepressant; Anticonvulsant; Neuroleptic;

Antianemic; Ophthalmological; Antithyroid; Cerebroprotective; Tranquilizer; Vasotropic; Cytostatic; Antiarrhythmic; Dermatological; Antilipemic; Muscular-Gen; Antimicrobial; Cardiant; Antisickling; Antiinfertility; Endocrine-Gen.

MECHANISM OF ACTION - Gene therapy; neurotransmitter transporter polypeptide modulator. No supporting data is given.

USE - (I) is useful for screening a compound for effectiveness as an agonist or antagonist of (I), by exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample. (I), the identified agonist and antagonist are useful for treating a disease or condition associated with decreased or overexpression of functional NTT in a patient. (I) is useful for screening for a compound that modulates the activity of the polypeptide or that binds to the polypeptide. (I) is further useful as an immunogen for preparing polyclonal or monoclonal antibody by hybridoma technology. (II) is useful for screening a compound for effectiveness in altering expression of a target polynucleotide comprising the sequence of (II). A probe comprising at least 20 contiguous nucleotides of (II) is useful for assessing toxicity of a test compound, by treating a biological sample containing nucleic acids with the test compound, hybridizing the probe with nucleic acids of the treated biological sample to form a complex, quantifying the amount of hybridization complex and comparing the complex in the treated biological sample with the amount of complex in an untreated biological sample, where a difference in the amount of complex in the treated biological sample is indicative of toxicity of the test compound. (IV) is useful for detecting the presence of (I) and purifying (I) from a sample. (IV), optionally labeled is useful for diagnosing a condition or disease associated with expression of NTT in a subject or in a biological sample (all claimed). (I) and (II) and modulators of (I) are useful for diagnosis, treatment and prevention of transport, neurological and psychiatric disorders. Transport disorders include akinesia, amyotrophic lateral sclerosis, ataxia telangiectasia, cystic fibrosis, Becker's muscular dystrophy, **diabetes** mellitus, **diabetes** insipidus, myasthenia gravis, myocarditis, Parkinson's disease, prostate cancer; cardiac disorders associated with transport include angina, bradyarrhythmia, dermatomyositis, polymyositis, neurological disorders associated with transport include Alzheimer's disease, amnesia, bipolar disorder, dementia, depression, epilepsy, Tourette's disorder, schizophrenia, and other disorders associated with transport include neurofibromatosis, sickle cell anemia, Wilson's disease, cataracts, infertility, hyperglycemia, hypoglycemia, Graves' disease, goiter, Cushing's disease, hypercholesterolemia and cystinuria. Neurological disorders treatable include epilepsy, stroke, Huntington's disease, dementia, and other extrapyramidal disorder, motor neuron disorders, prion disease including kuru, metabolic disease of the nervous system, and other developmental disorders of the central nervous system, neuromuscular disorders, metabolic, endocrine and toxic myopathies, periodic paralysis, mental disorders including mood and anxiety. Psychiatric disorders include acute stress disorder, alcohol dependence, anorexia nervosa, anxiety, obsessive-compulsive disorder, panic disorder and sleep disorder. (II) is useful for creating knock in humanized animals or transgenic animals to model human disease and to detect and quantify gene expression in biopsied tissues in which expression of NTT is correlated with disease. (II) is also useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence and oligonucleotide primers derived from (II) are useful to detect single nucleotide polymorphisms. NTT, fragments of it and antibodies specific for NTT are useful as elements on a microarray which is useful to monitor or measure **protein-protein** interactions, **drug-target** interactions and gene expression profiles. Sequences of (I) are used to analyze the **proteome** of a tissue or cell type.

Dwg.0/0

L155 ANSWER 44 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-034502 [04] WPIDS
DOC. NO. CPI: C2002-009699
TITLE: New human RNA metabolism protein for diagnosing or treating nervous system disorders, autoimmune/inflammatory disorders, cell proliferative disorders and developmental disorders.
DERWENT CLASS: B04 D16
INVENTOR(S): AU-YOUNG, J; AZIMZAI, Y; BATRA, S; BAUGHN, M R; BURFORD, N; HILLMAN, J L; LAL, P; LU, D A M; POLICKY, J J; TANG, Y T; YAO, M G; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001083524	A2	20011108	(200204)*	EN	196

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001057427	A	20011112	(200222)		
EP 1278843	A2	20030129	(200310)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001083524	A2	WO 2001-US13862	20010427
AU 2001057427	A	AU 2001-57427	20010427
EP 1278843	A2	EP 2001-930939	20010427
		WO 2001-US13862	20010427

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001057427	A	Based on	WO 200183524
EP 1278843	A2	Based on	WO 200183524

PRIORITY APPLN. INFO: US 2000-220553P 20000725; US 2000-200184P 20000428; US 2000-201875P 20000504; US 2000-202090P 20000504; US 2000-210232P 20000606

AB WO 200183524 A UPAB: 20020117
NOVELTY - An isolated human RNA metabolism protein (RMEP) (I), comprising 1 of 47 sequences (S1), given in the specification, a naturally occurring polypeptide comprising a sequence with 90 % identity to S1, or a biologically active or immunogenic fragment of S1, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polynucleotide (II) encoding (I);
(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);
(3) a cell transformed with (III);
(4) a transgenic organism comprising (III);
(5) production of (I);
(6) an isolated antibody (IV) that binds to (I);
(7) an isolated polynucleotide (V) comprising 1 of 47 sequences (S2),

given in the specification, a naturally occurring polynucleotide sequence with 90 % identity to S2, a complementary sequence, or a RNA equivalent;

(8) an isolated polynucleotide (VI) comprising 60 contiguous nucleotides of (V);

(9) detection (M1) of (V) in a sample, involving:

(a) hybridizing the sample with a probe comprising 20 contiguous nucleotides of a sequence complementary to (V) to form a hybridization complex, and detecting the presence, absence and amount (optional) of the hybridization complex; or

(b) amplifying (V) or its fragment using a polymerase chain reaction (PCR) and detecting the presence, absence, or amount of the amplified target polynucleotide or its fragment;

(10) a composition (VII) comprising (I), an agonist or an antagonist compound identified by using (I);

(11) preparing (M2) a polyclonal antibody to (IV), by:

(i) immunizing an animal with (I), or its immunogenic fragment;

(ii) isolating antibodies from the animal; and

(iii) screening the isolated antibodies with (I) to identify a polyclonal antibody specific to (I);

(12) an antibody (VIII) produced by M2;

(13) making (M3) a monoclonal antibody to (IV), by:

(i) immunizing an animal with (I), or its immunogenic fragment;

(ii) isolating antibody producing cells from the animal and fusing them with immortalized cells to form monoclonal antibody-producing hybridoma cells;

(iii) culturing the hybridoma cells; and

(iv) isolating the monoclonal antibody specific to (I);

(14) a monoclonal antibody (IX) produced by M3; and

(15) a composition (X) comprising (IV), (VIII) or (IX).

ACTIVITY - Anticonvulsant; cerebroprotective; nootropic; neuroprotective; antiparkinsonian; tranquilizer; neuroleptic; anti-HIV; antiallergic; antianemic; antiasthmatic; antiarteriosclerotic; antiinflammatory; **antidiabetic**; nephrotropic; antithyroid; immunosuppressive; thyromimetic; osteopathic; **antiarthritic**; antirheumatic; uropathic; ophthalmological; dermatological; antiulcer; cytostatic; hepatotropic; antipsoriatic.

MECHANISM OF ACTION - Gene therapy; vaccine. No biological data is given.

USE - (I) is useful for:

(a) screening a compound for effectiveness as an agonist;

(b) screening a compound for effectiveness as an antagonist;

(c) screening a compound that specifically binds (I);

(d) screening a compound that modulates the activity of (I);

A nucleic acid (II) encoding (I) is used for screening a compound for effectiveness in altering expression of a target polynucleotide comprising S2.

The nucleic acid (VI) is used for assessing toxicity of a test compound.

An antibody (IV) to (I) is used in a diagnostic test for a condition or a disease associated with the expression of RMEP in a biological sample.

(IV) is used for detecting (I) in a sample. (IV) is used for purifying (I) from a sample. A composition (VII) comprising (I) or an agonist or antagonist is used for treating a disease or condition associated with decreased or increased expression of functional RMEP. An antibody composition (X) is used for diagnosing a condition or disease associated with the expression of RMEP in a subject (all claimed).

(I) and (II) are used for diagnosing, treating and preventing:

(a) nervous system disorders such as epilepsy, stroke, Alzheimer's disease, Huntington's disease, dementia, Parkinson's disease;

(b) prion diseases such as Creutzfeldt-Jakob disease;

(c) fatal familial insomnia, nutritional and metabolic diseases of the nervous system;

(d) inherited, metabolic, endocrine, and toxic myopathy;
(e) a mental disorder including mood, anxiety, and schizophrenic disorders;
(f) amnesia and Tourette's disorder;
(g) autoimmune/inflammatory disorders such as acquired immunodeficiency syndrome (AIDS), allergies, anemia, asthma, atherosclerosis, Crohn's disease, diabetes mellitus, glomerulonephritis, gout, Hashimoto's thyroiditis, multiple sclerosis, osteoarthritis, osteoporosis, pancreatitis, rheumatoid arthritis, systemic lupus erythematosus, ulcerative colitis, and infections;
(h) cell proliferative disorders such as arteriosclerosis, cirrhosis, hepatitis, psoriasis, and cancer; and
(i) developmental disorders such as renal tubular acidosis.
(I) is used in a number of drug screening techniques, and to analyze the proteome of a tissue or cell type. (II) is used for creating knockin humanized animals or transgenic animals to model human diseases. (II) is used in somatic or germline gene therapy, and to generate a transcript image of a tissue or cell type. (II) is used for detecting differences in chromosomal location due to e.g. translocation or inversion among normal, carrier or affected individuals. (II) is used as hybridization probes for mapping naturally occurring genomic sequences.
Dwg.0/0

L155 ANSWER 45 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-010942 [01] WPIDS
CROSS REFERENCE: 2002-097342 [13]; 2002-499091 [53]; 2002-626184 [67]
DOC. NO. NON-CPI: N2002-009086
DOC. NO. CPI: C2002-002761
TITLE: Screening for bioactivity of candidate compound towards target proteins in mixture, useful for generating large number of **drug** molecules, comprises combining probe with mixture and sequestering proteins conjugated to probe.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): ADAM, G; CRAVATT, B F; LOVATO, M; PATRICELLI, M; SORENSEN, E
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001077668	A2	20011018	(200201)*	EN	118

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001024349 A 20011023 (200213)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001077668	A2	WO 2000-US34167	20001215
AU 2001024349	A	AU 2001-24349	20001215

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001024349	A	Based on	WO 200177668

PRIORITY APPLN. INFO: US 2000-222532P 20000802; US 2000-195954P 20000410; US 2000-212891P 20000620

AB WO 200177668 A UPAB: 20021022

NOVELTY - Screening for the bioactivity of candidate compound toward a group of related **target proteins** in **proteomic** mixture of **proteins** from cell comprising:

(a) combining a probe with an untreated portion and a portion inactivated with a non-covalent agent;

(b) sequestering proteins conjugated with the probe;

(c) determining the proteins that are sequestered; and

(d) comparing amount of the proteins sequestered, is new.

DETAILED DESCRIPTION - Screening (M1) for the bioactivity of a candidate compound toward a group of related **target proteins** in a **proteomic** mixture of proteins from a cell, by employing at least one probe comprising:

(a) combining at least one probe with an untreated portion and with a portion inactivated with a non-covalent agent, of the mixture under conditions for reaction with the **target proteins**;

(b) sequestering proteins conjugated with the probe from each of the mixtures;

(c) determining the proteins that are sequestered; and

(d) comparing the amount of each of the proteins sequestered from the untreated portion and the inactivated portion as indicative of the bioactivity of the candidate compound with the **target proteins**. The probe comprises a reactive functionality group specific for the group of **target proteins** and a ligand.

INDEPENDENT CLAIMS are also included for the following:

(1) screening for the bioactivity of a candidate compound toward a group of related **target** enzymes in a **proteomic** mixture of proteins from a cell employing at least one probe of formula R asterisk (F-L)-X (I) comprising M1;

(2) determining in a **proteomic** mixture (A) the presence of active **target** members (B) comprising a group of related proteins involving:

(a) combining (A) in wild-type form with a probe;

(b) combining (A) after non-specific deactivation with the probe; and

(c) determining the presence of (B) conjugated with the probe in (A) in active and inactive form, where the probe comprises a reactive functionality specific for the active site when active, under conditions for conjugation of the probe to (B) and when the probe conjugated to (B) in (A) in active form and in less amount in inactive form, the presence of (B) is determined;

(3) determining in a plurality of **proteomic** mixtures the presence of active **target** members of a group of related proteins which have a common functionality for conjugation at an active site comprising:

(a) combining the mixtures in wild type form with a probe containing a reactive functionality specific for the active site;

(b) determining the presence of target members conjugated with the probe; and

(c) analyzing for the presence of target members conjugated with the probe using simultaneous individual capillary electrokinetic analysis or capillary high performance liquid chromatography (HPLC), where when the target members are conjugated to target members, the presence of active target members is determined;

(4) determining in a **proteomic** mixture the presence of active **target** members of a group of related enzymes which have common functionality for conjugation at an active site comprising:

(a) combining the mixture in wild type form with a probe containing a reactive functionality specific for the active site;

(b) combining the mixture after non-specific deactivation with the

probe;

(c) determining the presence of **target** members conjugated with the probe in the **proteomic** mixtures in active and inactive form, where the probe is conjugated to at least one target member in the mixture in active form and in lesser amount in inactive form, the presence of active members is determined;

(5) a system for identifying active **target proteins** in a related group of proteins in a sample, using at least one activity-based probe (ABP) binding to several members of the proteins comprising:

(a) a sample containing at least one of the **target protein;**

(b) ABP of formula R asterisk (Q-L)-X (II); and

(c) a programmed data processor for receiving and transmitting values comprising a program for evaluating results from the combining of ABP and sample resulting in formation of conjugates with active **target proteins** present to determine the presence of active **target proteins** and providing a profile of the binding;

(6) a system for determining the status of a biological system in relation to the presence of members of at least one related group of active proteins, by employing the results from combining (I) and a sample suspected of containing at least one **target protein,** to produce conjugates of (I) with the **target proteins** in varying amounts in relation to the amount of each of the active **target proteins.**

X = a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality for adding a ligand;

L = a linking group, which is the same in each of the members of a library;

Q = a functional group reactive at an active site of a target protein, and is the same reactive functionality in each of the members of the library (preferably a sulfonyl group, fluorophosphonyl or fluorophosphoryl group); and

R asterisk = H or a moiety of less than 1 kDa providing specific affinity for the target protein;

asterisk = intends that R is a part of F or L.

F = functional group reactive at an active site of a target enzyme and is the same reactive functionality in each of the members of the library.

USE - For screening for the bioactivity of a candidate compound towards a group of related target proteins; e.g. for determining the status of a biological system in relation to the presence of the active protein; such as an infectious disease, a response to a therapeutic agent or a response to a candidate drug (claimed). The method is also useful for rapidly generating and developing large numbers of drug candidate molecules or for randomly generating a large number of drug candidates and later optimizing those candidates that show the most medicinal promise; for systemically synthesizing a large number of molecules that may vary greatly in their chemical structure or composition or that may vary in minor aspects of their chemical structure or composition. The screened compounds can be used to indicate the presence of a particular disease in a human or animal, the compounds can stimulate or inhibit the activity of bacteria, viruses, fungi or other infectious agent and/or modulate the effect of a disease by preventing or decreasing the severity of disease or curing a disease such as cancer, diabetes, atherosclerosis, high blood pressure, Parkinson's disease and other disease states.

ADVANTAGE - The method easily identifies the biological target molecule for lead compounds, all with varying ability to block cell division. The method shows whether the multiple lead compounds interact with the same or different biological target molecules. The method is simple, takes less time and is economical.

Dwg.0/24

L155 ANSWER 46 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-418080 [44] WPIDS
DOC. NO. NON-CPI: N2001-309733
DOC. NO. CPI: C2001-126433
TITLE: Novel human protease proteins (PRTS) useful for diagnosing, treating, preventing gastrointestinal, cardiovascular, autoimmune/inflammatory, cell proliferative disorders associated with abnormal expression of PRTS.
DERWENT CLASS: B04 D16 P14 S03
INVENTOR(S): AU-YOUNG, J; BAUGHN, M R; BURFORD, N; LAL, P; LU, D A M; NGUYEN, D B; REDDY, R; TANG, Y T; YANG, J; YAO, M G; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001046443	A2	20010628	(200144)*	EN	129

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001022857	A	20010703	(200164)	
EP 1240335	A2	20020918	(200269)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001046443	A2	WO 2000-US34811	20001219
AU 2001022857	A	AU 2001-22857	20001219
EP 1240335	A2	EP 2000-986665	20001219
		WO 2000-US34811	20001219

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001022857	A	Based on	WO 200146443
EP 1240335	A2	Based on	WO 200146443

PRIORITY APPLN. INFO: US 2000-179903P 20000202; US 1999-172055P 19991223; US 2000-177334P 20000121; US 2000-178884P 20000128

AB WO 200146443 A UPAB: 20010809
NOVELTY - Isolated human protease proteins (I) (referred as PRTS 1-14) having fully defined sequence (PS) of 1055, 358, 467, 187, 289, 960, 525, 795, 919, 209, 77, 414, 397 or 145 (S1-S14) amino acids as given in specification, a naturally occurring amino acid sequence having 90% sequence identity to PS, or biologically active or immunogenic fragment of PS, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polynucleotide (II) encoding (I);
(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) a cell (IV) transformed with (III);
(4) a transgenic organism comprising (III);
(5) preparation of (I);
(6) an isolated antibody that specifically binds to (I);
(7) an isolated polynucleotide (N1) comprising a sequence selected from:
(a) a polynucleotide sequence selected from a fully defined sequence of 4028, 1422, 1911, 854, 1386, 3323, 2123, 2893, 4170, 767, 1538, 1497, 1194 (S15-S27) or 438 (S28) nucleotides as given in the specification;
(b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide selected from S15-S28;
(c) a polynucleotide sequence complementary to the sequence of (a) or (b);
(d) an RNA equivalent of (a) to (c);
(8) an isolated polynucleotide comprising 60 contiguous nucleotides of N1;
(9) detecting a target polynucleotide in a sample which comprises a sequence of N1 involves:
(a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides which is complementary to the target polynucleotide in the sample and which specifically hybridizes to the target polynucleotide, under conditions, by which a hybridization complex is formed between the probe and the target polynucleotide or its fragments, and then detecting the presence or absence of the hybridization complex, and, optionally, if present the amount of the target polynucleotide is also quantitated; or
(b) amplifying the target polynucleotide or its fragments by polymerase chain reaction (PCR) and then detecting the presence or absence of the amplified target polynucleotide or its fragment optionally, if present the amount of the target polynucleotide is also quantitated;
(10) screening a compound for effectiveness as an agonist or antagonist of (I) involves exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample;
(11) screening for a compound that specifically binds to (I) involves combining (I) with a test compound under suitable conditions and then detecting binding of (I) to the test compound, thus identifying a compound that specifically binds to (I);
(12) screening for a compound that modulates the activity of (I) involves combining (I) with a test compound under conditions permissive for the activity of (I), assessing the activity of (I) in the presence of the test compound and then comparing the activity of (I) in the presence of test compound with the activity of (I) in the absence of the test compound, where a change in the activity of (I) in the presence of the test compound is indicative of a compound that modulates the activity of (I);
(13) screening a compound for effectiveness in altering expression of a target polynucleotide which comprises a sequence of (S15)-(S27) or (S28) involves exposing the sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide and comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound; and
(14) a method for assessing toxicity of a test compound, comprising:
(a) treating a biological sample containing nucleic acids with the test compound;
(b) hybridizing the nucleic acids of the sample with a probe comprising at least 20 contiguous nucleotides of N1 under conditions where a specific hybridization complex is formed between the probe and target polynucleotide, where the target polynucleotide comprises a sequence of N1 or its fragment;
(c) quantifying the amount of hybridization complex;
(d) comparing the amount of complex in the treated sample with the amount of complex in an untreated sample, where a difference in the

amounts is indicative of toxicity of the test compound.

ACTIVITY - Antiinflammatory; cytostatic; antiatherosclerotic; hypotensive; antitumor; cardiant; anti-HIV; immunosuppressive; dermatological; neuroprotective; antiviral; nootropic; antibacterial; antiinfertility. No supporting biological data is given.

MECHANISM OF ACTION - PRTS expression or activity modulators; gene therapy.

No supporting biological data is given.

USE - The pharmaceutical compositions comprising (I) or an agonist of (I) is useful for treating a disease or condition associated with decreased expression of functional PRTS. The pharmaceutical composition comprising the antagonist of (I) is useful for treating a disease or condition associated with overexpression of (I). (I) is useful for identifying compounds that bind to (I) or which modulate activity of (I).

(I) and (II) are useful for diagnosing, treating or preventing a gastrointestinal disorder such as anorexia, cardiovascular disorder such as atherosclerosis and hypertension, autoimmune/inflammatory disorders such as acquired immuno deficiency syndrome (AIDS), cell proliferative disorders such as actinic keratosis, a developmental disorders such as epilepsy, an epithelial disorders such as allergic contact dermatitis, neurological disorders such as Alzheimer's disease, and reproductive disorders such as infertility.

(II) is useful for creating knock out or knock in humanized animals or transgenic animals to model human disease. (II) is useful for somatic or germline gene therapy for treating the above mentioned disorders. (II) is also useful for developing genetic linkage maps, detecting differences in chromosomal location due to translocation, inversion etc.

(I), its catalytic or immunogenic fragments are useful for screening libraries of compounds in several drug screening assays. (I) is useful for analyzing the proteome of a tissue or cell type.

Antibodies which bind to (I) may be used for diagnosis of disorders characterized by expression of (I) or in assays to monitor patients being treated with PRTS or agonists, antagonists or inhibitors of PRTS. The antibodies specific for PRTS, or PRTS or its fragments may be used as elements on a microarray which is useful to monitor protein-protein interaction, drug-target interaction, etc. The antibodies are also useful for assessing toxicity of a test compound. The method involves treating biological sample containing protein with the test compound and incubating with antibodies specific to the PRTS polypeptides.

Dwg.0/0

L155 ANSWER 47 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-390243 [41] WPIDS
DOC. NO. CPI: C2001-118895
TITLE: Novel human lyase proteins (HLYAP) useful for diagnosing, treating and preventing neurological, reproductive, cell proliferative and inflammatory disorders associated with abnormal expression of HLYAP.
DERWENT CLASS: B04 D16
INVENTOR(S): BANDMAN, O; BAUGHN, M R; HILLMAN, J L; LU, D A M; TANG, Y T; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001044445	A2	20010621	(200141)*	EN	102

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001024309 A 20010625 (200162)
EP 1242590 A2 20020925 (200271) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001044445	A2	WO 2000-US33815	20001213
AU 2001024309	A	AU 2001-24309	20001213
EP 1242590	A2	EP 2000-988059	20001213
		WO 2000-US33815	20001213

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001024309	A	Based on	WO 200144445
EP 1242590	A2	Based on	WO 200144445

PRIORITY APPLN. INFO: US 1999-172307P 19991216

AB WO 200144445 A UPAB: 20010724
NOVELTY - Isolated human lyase proteins (I) (referred as HLYAP 1-10) having defined sequence (PS) of 243, 425, 216, 343, 74, 176, 374, 780, 594 or 298 amino acids given in specification, a naturally occurring amino acid sequence having 90% sequence identity to PS, or biologically active or immunogenic fragment of PS, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated polynucleotide (II) encoding (I). (II) comprises a defined sequence of 1686, 2053, 2490, 1230, 955, 849, 1919, 2735, 2822 (S11-S19) or 1774 (S20) nucleotides given in the specification, is a naturally occurring polynucleotide sequence having 90% identity to the above mentioned polynucleotide sequences, a polynucleotide sequence which is complementary to the above mentioned sequences, or is a RNA equivalent of the above mentioned sequences;

(2) recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) cell (IV) transformed with (III);

(4) transgenic organism comprising (III);

(5) preparation of (I);

(6) isolated antibody that specifically binds to (I);

(7) detecting a target polynucleotide in a sample which comprises a sequence of (II) comprising hybridizing the sample with a probe containing at least 20 contiguous nucleotides which is complementary to the target polynucleotide in the sample and which specifically hybridizes to the target polynucleotide, under conditions, by which a hybridization complex is formed between the probe and the target polynucleotide or its fragments, and then detecting the presence or absence of the hybridization complex, and, optionally, if present the amount of the target polynucleotide is also quantitated. Alternately, the method is carried out by amplifying the target polynucleotide or its fragments by polymerase chain reaction (PCR) and then detecting the presence or absence of the target polynucleotide or its fragment;

(8) isolated polynucleotide comprising 60 contiguous nucleotides of (II);

(9) screening a compound for effectiveness as an agonist or antagonist of (I) comprising exposing a sample containing (I) to a compound and detecting agonist or antagonist activity in the sample;

(10) screening for a compound that specifically binds to (I) comprising combining (I) with a test compound under suitable conditions

and then detecting binding of (I) to the test compound, thus identifying a compound that specifically binds to (I);

(11) screening for a compound that modulates the activity of (I) comprising combining (I) with a test compound under conditions permissive for the activity of (I), assessing the activity of (I) in the presence of the test compound and then comparing the activity of (I) in the presence of test compound with the activity of (I) in the absence of the test compound. A change in the activity of (I) in the presence of the test compound is indicative of a compound that modulates the activity of (I); and

(12) screening a compound for effectiveness in altering expression of a target polynucleotide which comprises a sequence of (S11)-(S19) or (S20) comprising exposing the sample containing the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide and comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

ACTIVITY - Antiarteriosclerotic; antiatherosclerotic; antiinflammatory; antipsoriatic; cytostatic; hepatotrophic; immunosuppressive; antiinfertility; gynecological; osteopathic; anticonvulsant; cerebroprotective; nootropic; neuroprotective; antiparkinsonian; tranquilizer; neuroleptic; anti-HIV; dermatological; antiallergic; antianemic; antiasthmatic; nephrotophic; antigout; **antiarthritic**; antirheumatic; antiulcer; ophthalmological. No supporting data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful for identifying compounds that bind to (I) or which modulate activity of (I). (II) is useful for assessing toxicity of a test compound.

(I) and (II) are useful for diagnosing, treating or preventing cell proliferative disorders such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, psoriasis, mixed connective tissue disease (MCTD), myelofibrosis, a cancer such as adenocarcinoma, leukemia, lymphoma or melanoma; reproductive disorders such as infertility, ovulatory defects, disruption of the estrous cycle, disruptions of the menstrual cycle, endometrial and ovarian tumors, ectopic pregnancies and teratogenesis; neurological disorders such as epilepsy, stroke, Alzheimer's disease, Huntington's disease, Parkinson's disease, bacterial and viral meningitis, brain abscess, Creutzfeldt-Jakob disease, cerebral palsy, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, anxiety, amnesia, and schizophrenic disorders; inflammatory disorders such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, amyloidosis, anemia, asthma, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy and Crohn's disease, atopic dermatitis, Goodpasture's syndrome, gout, multiple sclerosis, **osteoarthritis**, **osteoporosis**, psoriasis, rheumatoid **arthritis** or ulcerative colitis and uveitis.

(II) is useful to detect upstream sequences such as promoters and regulatory elements. (II) is useful for creating knock out or knock in humanized animals or transgenic animals to model human disease. (II) is useful for somatic or germline gene therapy for treating the above disorders. Oligonucleotide primers derived from (II) may be used to detect single nucleotide polymorphisms. (II) may be used for generating hybridization probes useful in mapping the naturally occurring genomic sequences. (II) is useful for developing genetic linkage maps, detecting differences in chromosomal location due to translocation or inversion. Oligonucleotides or longer fragments derived from any of the polynucleotide sequences may be used as elements on a microarray. (I), its catalytic or immunogenic fragments are useful for screening libraries of compounds in several drug screening assays. (I) is useful for analyzing

the **proteome** of a tissue or cell type. A vector encoding (I) or its fragments is useful for treating the above mentioned disorders. Antibodies which bind to (I) may be used for diagnosis of disorders characterized by expression of (I) or in assays to monitor patients being treated with HLYAP or agonists, antagonists or inhibitors of HLYAP. The antibodies specific for HLYAP may be used as elements on a microarray which is useful to monitor **protein** interaction and **drug -target** interaction. The antibodies are also useful for assessing toxicity of a test compound.
Dwg.0/0

L155 ANSWER 48 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-244811 [25] WPIDS
DOC. NO. NON-CPI: N2001-174296
DOC. NO. CPI: C2001-073482
TITLE: Novel human protein phosphatase and kinase proteins for diagnosis, treatment and prevention of gastrointestinal, immune system, neurological and cell proliferative disorders.
DERWENT CLASS: B04 D16 P14 S03
INVENTOR(S): AZIMZAI, Y; BANDMAN, O; BAUGHN, M R; HILLMAN, J L; LU, D A M; TANG, Y T; YUE, H
PATENT ASSIGNEE(S): (INCY-N) INCYTE GENOMICS INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001020004	A2	20010322	(200125)*	EN	103

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000078297	A		20010417	(200140)	
EP 1212436	A2		20020612	(200239)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001020004	A2	WO 2000-US25515	20000914
AU 2000078297	A	AU 2000-78297	20000914
EP 1212436	A2	EP 2000-968368	20000914
		WO 2000-US25515	20000914

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000078297	A	Based on	WO 200120004
EP 1212436	A2	Based on	WO 200120004

PRIORITY APPLN. INFO: US 1999-154141P 19990915
AB WO 200120004 A UPAB: 20011129
NOVELTY - An isolated human protein phosphatase and kinase proteins (PPHKP) (I) comprising a 329, 141, 447, 666, 358, 470, 150, 253, 442, 659 or 145 residue amino acid sequence (S1), fully defined in the specification, a naturally occurrence sequence having at least 90 % identity to S1, and biologically active and immunogenic fragments of S1,

is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I);

(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) a cell (IV) transformed with (III);

(4) a transgenic organism (V) comprising (III);

(5) production of (I), comprising culturing (IV) under expression conditions, and recovering the polypeptide;

(6) an isolated antibody (VI) which specifically binds to (I);

(7) an isolated polynucleotide (VII) comprising a 1884, 784, 1657, 2118, 2116, 2897, 839, 1081, 2924, 2781 or 754 base pair sequence (S2), fully defined in the specification, a naturally occurrence sequence having at least 90 % identity to (S2), its complement, or an RNA equivalent;

(8) an isolated polynucleotide (VIII) comprising at least 60 contiguous nucleotides of (VII);

(9) detecting (M1) a target polynucleotide having a sequence of (VII) in a sample, comprising:

(a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides of a sequence complementary to the target polynucleotide in the sample, the probe specifically hybridizes to the target polynucleotide under hybridizing conditions, and detecting the presence or absence of the hybridization complex, and, optionally, if present, the amount; or

(b) amplifying the target polynucleotide or its fragment using polymerase chain reaction amplification, and detecting the presence or absence of the amplified target polynucleotide or its fragment, and optionally, if present, the amount;

(10) screening (M2) a compound for effectiveness as an agonist or antagonist of (I) or for effectiveness in altering the expression of a target nucleotide having a sequence of (II), comprising:

(a) exposing a sample comprising (I) or the target nucleotide to the compound;

(b) detecting agonist or antagonist activity in the sample or the altered expression of the target nucleotide; and

(c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound;

(11) screening (M3) for a compound that specifically binds to (I) or modulates the activity of (I), comprising:

(a) combining (I) with at least one test compound and detecting binding of (I) to the test compound, identifying a compound that specifically binds to (I), or

(b) assessing the activity of (I) in the test sample, and comparing the activity of (I) in the presence and absence of the test compound, a change in the activity of (I) in the presence of the test compound indicates a compound that modulates the activity of (I);

(12) a composition (IX) comprising (I), or an agonist or antagonist of (I) identified by M2; and

(13) assessing (M4) toxicity of a test compound, comprising:

(a) treating a biological sample containing nucleic acids with the test compound;

(b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of (VII) under hybridizing conditions, the target polynucleotide comprising a polynucleotide sequence of (VII) or its fragment;

(c) quantifying the amount of hybridization complex; and

(d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, a difference indicates the toxicity of the test compound.

ACTIVITY - Antiinflammatory; antidiarrheic; laxative; antiemetic;

hepatotropic; anti-HIV (human immunodeficiency virus); antianemic; antiasthamatic; antiarteriosclerotic; antithyroid; immunosuppressive; **antidiabetic**; nephrotropic; antigout; thyromimetic; neuroprotective; osteopathic; uropathic; ophthalmological; **antiarthritic**; antirheumatic; dermatological; cytostatic; antibacterial; antifungal; protozoacide; tranquilizer; vulnerary; anticonvulsant; cerebroprotective; antiParkinsonian; nootropic; neuroleptic; antipsoriatic.

MECHANISM OF ACTION - Gene therapy.

No biological data is given.

USE - (IX) is useful for treating a disease or condition associated with decreased expression or overexpression of PPHKP. (I) or its fragments useful to screen for compounds that bind to (I) or modulate the activity of (I). (All claimed). (I) and (II) are useful in diagnosis, treatment and prevention of gastrointestinal disorders such as dysphagia, dyspepsia, indigestion, gastritis, anorexia, nausea pyrosis, gastroenteritis, hepatitis, Crohn's disease, Whipple's disease, Mallory-Weiss syndrome, irritable bowel syndrome, diarrhea, constipation, jaundice Wilson's disease, Reye's syndrome; immune system disorders such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, anemia, asthma, atherosclerosis, autoimmune thyroiditis, diabetes mellitus, Good pasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, osteoporosis, pancreatitis, Reiter's syndrome, rheumatoid arthritis, Sjogren's syndrome, systemic lupus erythematosus, Werner syndrome, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; neurological disorders such as epilepsy, stroke, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease, kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, Tourette's disorder; and cell proliferative disorders such as bursitis, cirrhosis, psoriasis, leukemia, lymphoma, melanoma, myeloma, sarcoma, and cancer. (I) is useful for analyzing the proteome of a tissue or cell type and for screening libraries of compound in various drug screening techniques. (II) is useful in somatic or germline gene therapy and in diagnosis of that diseases. (II) is useful for creating transgenic humanized animals (pigs) or transgenic animals (mice or rats) to model human diseases. (II) is useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence. (VI) is useful for the diagnosis of disorders characterized by expression of PPHKP, or in assays to monitor patients being treated with PPHKP or agonist, antagonist or inhibitors of PPHKP. (VI) is useful as elements on a microarray which is useful to monitor or measure protein-protein interactions, drug-target interaction, and gene expression profiles.

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L155 ANSWER 49 OF 49 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-007027 [01] WPIDS
CROSS REFERENCE: 2002-488070 [52]
DOC. NO. NON-CPI: N2001-005048
DOC. NO. CPI: C2001-001701
TITLE: Novel methods for separating and identifying a polypeptide species from a sample solution by electrophoresis and mass spectrographic fragmentation, useful for preparing protein fingerprints.
DERWENT CLASS: B04 D16 J04 S03 T01
INVENTOR(S): HALL, M P; PETERSON, J N; PETESCH, R; SCHNEIDER, L V
PATENT ASSIGNEE(S): (TARG-N) TARGET DISCOVERY INC
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000063683	A1	20001026	(200101)*	EN	263

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000043624 A 20001102 (200107)
EP 1194768 A1 20020410 (200232) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000063683	A1	WO 2000-US10504	20000419
AU 2000043624	A	AU 2000-43624	20000419
EP 1194768	A1	EP 2000-923511	20000419
		WO 2000-US10504	20000419

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000043624	A	Based on	WO 200063683
EP 1194768	A1	Based on	WO 200063683

PRIORITY APPLN. INFO: US 2000-513907 20000225; US 1999-130238P 19990420; US 2000-513395 20000225; US 2000-513486 20000225

AB WO 200063683 A UPAB: 20020820
NOVELTY - Separating and identifying (I) a polypeptide species from a sample solution comprising electrophoresing the sample solution in a capillary electrophoresis (CE) device and obtaining a polypeptide sequence tag (PST) identifying the resolved species by mass spectrographic fragmentation of the eluted polypeptide species, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) identifying a high-resolution protein expression fingerprint for a cell type, tissue, or pathological sample comprising obtaining a protein-containing extract of a cellular sample, electrophoresing the extract, eluting protein-containing fractions, electrophoresing the fractions in a second apparatus (or apparatuses in parallel), identifying the species of proteins by mass spectroscopy to obtain PSTs, and compiling a dataset or fingerprint record containing the collection of PSTs;

(2) a computer system comprising a database including fingerprint records each comprising an array of at least 50 molecular species with a unique identifier cross-tabulated with quantitative data indicating relative and/or absolute abundance of each species in a sample, and a user interface capable of receiving at least 1 query to the database;

(3) producing or accessing a computer database comprising a computer and software for storing protein expression fingerprint records cross-tabulated with data specifying the source of the protein sample;

(4) labeling different proteins in a sample comprising contacting the sample with a labeling agent comprising a unique ion mass signature component, a quantitative detection component and a reactive functional group to covalently attach a label the at least a portion of the proteins;

(5) separating proteins in an initial sample comprising:

(a) performing electrophoretic methods in a series (each performed with a sample collected from the preceding method), each method comprising;

(i) electrophoresing a sample to obtain resolved proteins; and

(b) detecting resolved proteins;

(6) separating proteins by electrophoretic methods comprising:

(a) performing electrophoretic methods in series (each performed with a sample collected from the preceding method), each method comprising;

(i) withdrawing and collecting multiple fractions containing resolved proteins;

(b) labeling the proteins or protein in the collected fractions prior to the last electrophoretic method; and

(c) detecting proteins in the electrophoretic medium during the final electrophoretic method;

(7) separating proteins comprising:

(a) performing capillary electrophoretic methods (each performed with a sample collected from the preceding method), each method comprising;

(i) electrophoresing a sample of proteins; and

(ii) withdrawing and collecting multiple fractions of resolved proteins;

(b) labeling the protein or proteins in the collected fraction prior to the last electrophoretic method; and

(c) conducting a final CE method comprising detecting resolved protein within, or withdrawn from the final capillary;

(8) separating proteins in an initial sample comprising:

(a) performing capillary electrophoretic methods (each performed with a sample collected from the preceding method), each method comprising;

(i) electrophoresing a sample of proteins where fractions containing a subset of the proteins are isolated physically, temporally or spatially; and

(b) detecting isolated proteins;

(9) separating proteins comprising performing at least 2 capillary electrophoretic methods where a sample for the second method is obtained during the first and contains only a subset of the proteins in the initial sample;

(10) analyzing **metabolic pathways** comprising:

(a) administering a substrate labeled with a stable isotope at a known abundance to a subject;

(b) allowing the substrate to be at least partially metabolized by the subject; and

(c) determining the abundance of the isotope in a sample from the subject to determine a value of the flux of each target analyte;

(11) analyzing metabolic pathways comprising

(a) at least partially separating target analytes comprising substrates labeled with a stable isotope and/or at least 1 target metabolite resulting from the metabolism of the substrate by the subject from a sample, where the relative isotopic abundance is known; and

(b) determining the abundance of the isotope in target analytes to determine a value for the flux of each target analyte;

(12) screening for metabolites correlated with disease comprising:

(a) analyzing a sample comprising a substrate labeled with a stable isotope and/or at least 1 target metabolite resulting from the metabolism of the substrate by the subject from a sample, where the relative isotopic abundance is known at the time of administration and where the analyzing step comprises determining the isotopic abundance of the isotope in analytes to determine a value for the flux of each analyte; and

(b) comparing the flux values of the analytes with flux values for the same analytes obtained from a control subject;

(13) screening for the presence of a disease comprising:

(a) analyzing a sample comprising an isotopically labeled substrate or metabolite as in (12); and

(b) comparing the determined flux values with a range of values for that analyte;

(14) an apparatus for performing a method as in (I), (1), (4)-(8), and/or (10)-(13) comprising at least 2 CE devices fixed to a common platform or frame and in liquid communication with each other and with a mass spectrometer.

USE - The methods, apparatus, and computer systems are useful for carrying out proteomics and metabolic profiling on biological samples,

e.g. for diagnosing and/or monitoring disease conditions, for the identification of resolved protein samples and for identifying and quantifying the protein expression patterns (protein fingerprint) of cells, tissues and organs.

ADVANTAGE - The methods and apparatus have high sensitivity and can give protein fingerprints for cells, tissues and organs lacking sufficient resolution, precision, and/or sensitivity.

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